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ALEUKEMIC RETICULOSIS

AN ADDITIONAL MEMBER OF THE GROUP OF SO-CALLED CUTANEOUS LYMPHOBLASTOMAS

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To the great majority of American dermatologists the term cutaneous lymphoblastoma conveys a certain definite clinical picture. It consists usually of a preliminary diffuse dermatitis (generalized scaly erythroderma) succeeded by a tumor-like stage (granuloma fungoides *sensu stricto*). It is the clinical phase which commands the scene. Promptly after the appearance of the clinical manifestations, however, the picture becomes associated with disease of the lymphoid apparatus. Therefore, considerations of this subject must be arranged into, and must revolve around, two fields: (1) the essentially dermatologic and (2) the hematopoietic.

It is not urgent to discuss the former field because dermatologists are so familiar with it, but at present there is real need for better understanding of the precise scope of the lymphoblastoma. The rôle of the lymphocyte in particular is implied, for if the suffix is removed from "lymphoblastoma" only "lymphoblast" remains. Indeed it was the original intention of Mallory [1] to attach to the lymphoblastomas the sense of a malignant tumor process with only the lymphoblast as the cell performing. Warthin [2] followed his lead in nomenclature. In speaking of mycosis fungoides he said: "In the great majority of cases this disease is a small-celled lymphoblastoma." Yet if one pries into the premises a little more inquisitively one finds that Warthin vitiated

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1. Mallory, cited by Krumbhaar.[10]

2. Warthin, A. S.: The Genetic Neoplastic Relationships of Hodgkin's Disease, Aleukaemic and Leukaemic Lymphoblastoma, and Mycosis Fungoides, Ann. Surg. **93**:153 (Jan.) 1931.

such an exclusive rôle for the lymphocytic series when he included Hodgkin's disease among lymphoblastomas in general. In this light, then, there is a conflict between the etymology of "lymphoblastoma" and the range of cell types included in the various dermatoses constituting the group of cutaneous lymphoblastomas. Nevertheless, it appears fitting to concede that the term lymphoblastoma in the sense in which it was used by Warthin pertained to lesions in which it was essentially the lymphocyte which was concerned.

Twelve years ago Keim [3] formally introduced the term lymphoblastoma to American dermatologists in connection with a case of universal leukaemia cutis. Five years later he reported twenty cases under the same designation. In the interim Fraser [4] reported two cases of mycosis fungoides in which he was finally able to establish the diagnoses of lymphatic leukemia and lymphosarcoma. He affirmed Keim's opinion of the ". . . . genetic relation between mycosis fungoides, lymphatic leukemia and lymphosarcoma" but at the same time stated a preference for the name reticulum cell sarcoma rather than lymphosarcoma. This indicated at least that he recognized the participation of the reticulo-endothelial system likewise in mycosis fungoides, i. e., that he believed that mycosis fungoides was not exclusively a lesion of the lymphocyte.

Dermatologists are thus justified in taking Keim's two papers as base-lines (singularly, the first paper antedated Warthin's communication by seven years), with Frazer's paper interposed. If one follows Keim's theory there is little recourse but to accept the scope of cutaneous lymphoblastoma as he indicated it, as he and Warthin, to say nothing of Wile, were of the same Michigan school. There must have been the closest understanding between these three workers. Of lesser importance for present purposes is the fact that all lymphoblastomas, cutaneous or other, were emphatically classified as neoplastic processes—not as infections. It is significant in this connection that reticulosis was not mentioned in any case; evidently reticulum, if present (as in cases of Hodgkin's disease), was regarded as the reactive, normal stroma of the tissue which was being invaded by the supposedly neoplastic lymphocyte. Thereafter, Keim's statements, ". . . the multiple clinical pictures associated with true lymphadenoses should be

3. Keim, H. L.: Universal Leukemia Cutis, Arch. Dermat. & Syph. **10**:579 (Nov.) 1924; The Lymphoblastomas, ibid. **19**:533 (April) 1929.

4. Fraser, J. F.: Mycosis Fungoides, Arch. Dermat. & Syph. **12**:814 (Dec.) 1925.

5. Some hematologists at least hold a similar opinion. Pepper and Farley (Practical Hematological Diagnosis, Philadelphia, W. B. Saunders Company, 1933, p. 443) said of mycosis fungoides in their text: "It is probable that the hemopoietic disorder is primary, and the condition should be diagnosed according to the blood picture and the mycosis fungoides considered a secondary phenomenon."

regarded as the variable cutaneous expression of the lymphoblastomas," [5] and ". . . the constant pathologic condition in all is a cell of the lymphocyte series" were sufficiently definite, and they narrow the considerations to cells of the lymphocyte series, although it must be pointed out at once that this statement pertains only to the circumstances present in Keim's twenty cases.

In Keim's series little additional help, except in a negative way, was given from the observations on the bone marrow, although this is briefly described in some of his cases. The blood pictures too are described only briefly. We are of the opinion that in this large series of cases neither the blood nor the bone marrow was studied exhaustively in respect to cell types as considered by modern hematocytologists and that the observations are therefore not quite adequate to exclude the reticuloses from the lymphoblastomas. Future reports of cases of granuloma fungoides and of lymphoblastoma in general will be more valuable for analysis if the details of cytology of the blood, bone marrow, spleen, liver and lymph nodes are recorded in the splendid way in which both Loveman and Mercer reported their observations in their cases of leukemic reticulosis.

The preceding sentences are not intended as a criticism of the scope of the hematopoietic studies of the Michigan school, but they indicate that from the point of view of pathology the way is still open to include other members of the hematopoieses among the lymphoblastomas constituting Keim's series. If this can be done, it remains only to establish a similar set of clinical circumstances and join them with some vice of the blood-forming organs in order for the disease to qualify as a member of the group of lymphoblastomas. We believe that this can be done in the case which we report. We are of the opinion that the presence of a premycotic stage followed by a tumor stage and death satisfies the clinical requirements. Thereafter the profound alterations met in blood-forming tissues at necropsy, whether they are regarded as manifestations of atypical Hodgkin's disease, lymphosarcoma or reticulosis, complete the requirements of the lymphoblastomas.

We urge the reader to note the faithfulness with which the full scope of the pathologic changes of granuloma fungoides was exhibited on the skin of our patient, as illustrated by photographs. Incidentally, such was not the case in the instances of leukemic reticulosis (monocytic leukemia) reported by Mercer [6] and by Loveman,[7] who have so fully discussed the latter disease.

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6. Mercer, Samuel T.: The Dermatosis of Monocytic Leukemia, Arch. Dermat. & Syph. **31**:615 (May) 1935.

7. Loveman, Adolph B.: Monocytic Leukemia Cutis, South. M. J. **29**:357 (April) 1936.

REPORT OF A CASE

Course.—P. M., a 36 year old Filipino living in Hawaii, H. I., exhibited a generalized scaly erythroderma which began in November 1931. At first there was a patch of itchy dermatitis above the interscapular region; within a few days this extended to cover the entire body. Particularly affected were the face, ears and interscapular, antecubital and popliteal regions. The palms and soles alone were not involved. The lesions consisted of large slightly infiltrated furfuraceous and crusted erythematous plaques which were intensely pruritic. When the lesions were cleaned a raw red weeping surface remained. After three weeks of treatment by soothing measures the patient was discharged much improved.

In August 1932, i. e., nine months later, there was a mild recurrence accompanied by pruritus. In October the type of eruption changed; this time it involved both cheeks, the anterior portion of the chest, the extensor surface of both arms and the inside of the thighs. The lesions did not itch. They were discrete irregular reddish brown patches. The patient had been gradually losing weight, and he complained of malaise and weakness.

The cervical, axillary, epitrochlear and inguinal lymph nodes were slightly enlarged and firm but not tender. There were crepitant râles at both apexes posteriorly, and moderately advanced pulmonary tuberculosis was demonstrated. The spleen was enlarged, firm and tender. The ulnar nerves were palpable and somewhat tender; there appeared to be a greater wasting of the thenar, hypothenar and interosseous groups of muscles than could be accounted for by muscular inactivity. Neurologic examination revealed no abnormality in the sensory or motor system or in the reflexes.

There was thus a preliminary diffuse dermatitic stage extending, with one remission, over a period of one year. Then, promptly after the patient's admission to the hospital, widely generalized macules and subcutaneous nodules developed. The first, which were dime-sized, slightly elevated and bluish red, were located on the thoracic region. Their appearance was preceded by fever, the temperature reaching 101 F., which persisted until the patient's death.

The distribution of the subcutaneous swellings was similar to that of the diffuse eruption which preceded them, i. e., they were present over the ears, cheeks, middle of the forehead, tip of the nose, extensor surfaces of the arms, upper parts of the chest, both anteriorly and posteriorly, inner aspect of the thighs and legs. They varied in size, one on the right cheek being as large as a pigeon egg. They were fairly firm, dusky or livid and not ulcerated. Eventually they became firmly attached to the skin.

During the third week of the tumor stage symptoms of laryngeal edema necessitated tracheotomy. There was intermittent swelling of the wrist and joints, associated with severe pain over the joints and over the small bones of the hands and feet. In spite of repeated blood transfusions, roentgen therapy and hypodermic administration of iron and arsenic, the patient became progressively more anemic and toxic. He died on Jan. 27, 1933, after a slight pulmonary hemorrhage, in the fifteenth month of the disease and the ninth week of the tumor stage.

Laboratory Studies.—The Wassermann and Kahn tests of the blood were negative. The number of red blood cells was always below 3,000,000. There was moderate leukopenia. The percentage of polymorphonuclears averaged from 65 to 89; that of mononuclears, 2, and that of lymphocytes, 9. Abnormal cells were not observed.

Tubercle bacilli were noted in the sputum on three occasions; they were established as such by inoculation of guinea-pigs. A culture of the blood gave negative

results. Repeated smears from the nose and from snips of tissue from lesions, including the subcutaneous nodules, did not show Hansen's bacillus. The non-protein nitrogen content of the blood was 27.2 mg. per hundred cubic centimeters; the uric acid content was 3.5 mg., and the sugar content, 106 mg. The urine contained albumin and casts but no Bence-Jones protein.

Histologic sections of skin, subcutaneous nodules and cervical lymph nodes exhibited similar features, namely, groups of endothelial-like cells which in the cutaneous sections were just beneath the intact epithelium. There were zones of round cells in alveolar-like arrangement, varying in size, shape and staining intensity. There was no evidence of a purely inflammatory involvement, and the histologic picture did not resemble that of granuloma. The histologic diagnosis was lymphosarcomatosis.

Roentgen Studies.—In the chest in addition to signs of fibroid tuberculosis there was definite widening of the superior mediastinum, which was doubtless referable to glandular enlargement. The sternum, clavicle and ribs were normal. In the

Fig. 1.—Tumor stage just before death.

skull there was definite rarefaction in the left frontoparietal and to a slight degree in the occipital region. The posterior sutures were widened. The left foot showed two or three slight periosteal elevations, generalized atrophy due to disuse and moderate rarefaction of the medullary canal in the proximal phalanx of the middle toe. There was definite destruction of bone in the second phalanx of the great toe. The hands showed corresponding changes: There was rarefaction of the medullary canal of all the phalanges and metacarpals, the change being particularly at the extremities but extending into the medullary canal of most of the bones. There was destruction of the distal end of the first phalanx of the middle finger. Some of the metacarpals exhibited sclerosis in places. As to the radius and ulna, there was slight destruction of bone at their lower extremities, on both the right and the left side, and the rarefaction extended into the medullary canal. There was periosteal thickening at the middle. Roentgenograms of the pelvis showed only sclerosis of the left sacro-iliac joint; the vertebrae were normal.

In short, there was clearcut evidence of infiltration of both the cortex and the medulla, with actual destruction of bone in some places. The bones of the toes, hands and wrists suffered most, but the skull and tibia were also involved.

Gross Postmortem Examination.—The patient was markedly emaciated. The subcutaneous nodules were firm and grayish white on the surface of the sections. There was a cavity in the upper part of the right lung showing signs of recent hemorrhage. There were tubercles in the upper lobes of both lungs. The heart was small and pale. The spleen was the size of a small cantaloup; it was firm and contained one large grayish white nodule. Both of the testes contained numerous nodules. The inner surface of the left temporal bone contained nodular masses which were not attached to the dura. The distal portion of the left radius and that of the ulna showed extensive destruction immediately underneath tumor-like masses of the periosteum. The second toe of the right foot was similarly affected. Section of the peripheral nerves revealed no abnormalities.

Microscopic Studies.—Sections from the following structures were stained with hematoxylin and eosin, Mallory's connective tissue stain and azure II and eosin:

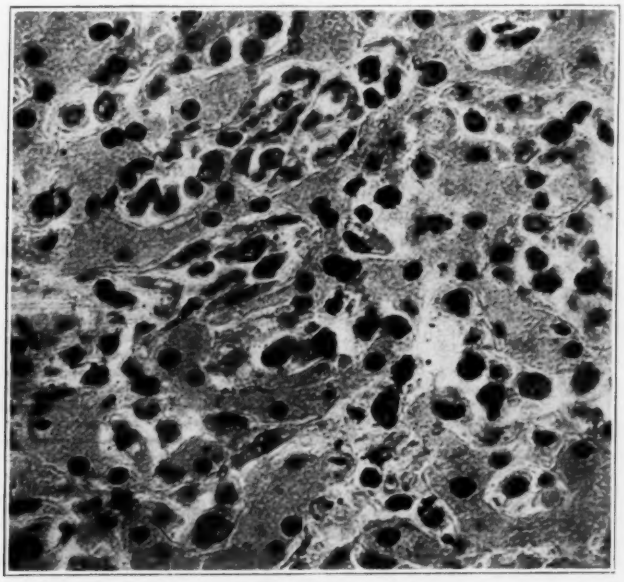

Fig. 2.—Section of liver showing monocytes in the sinuses and proliferation of Kupffer cells.

lung, liver (two specimens), spleen (two specimens), lymph nodes (four specimens), periosteum (two specimens), bone (two specimens) and skin (three specimens).

Lung: Only the picture of fibrocaseous tuberculosis was observed. The endothelioid cells were normal; i. e., the general reticulo-endothelioid state appeared to have had no modifying influence on these reactive cells against the tuberculous irritant.

Liver: There was no fibrosis, nor was there any important degeneration of the parenchymal cells. In the perilobular fibrous tissue there were occasional rather large infiltrations of small lymphocytes with a minor intermixture of monocytes. Most conspicuous was the fact that invariably monocytes were present in the sinusoids; they were most abundant at the centers of the lobules. There was no

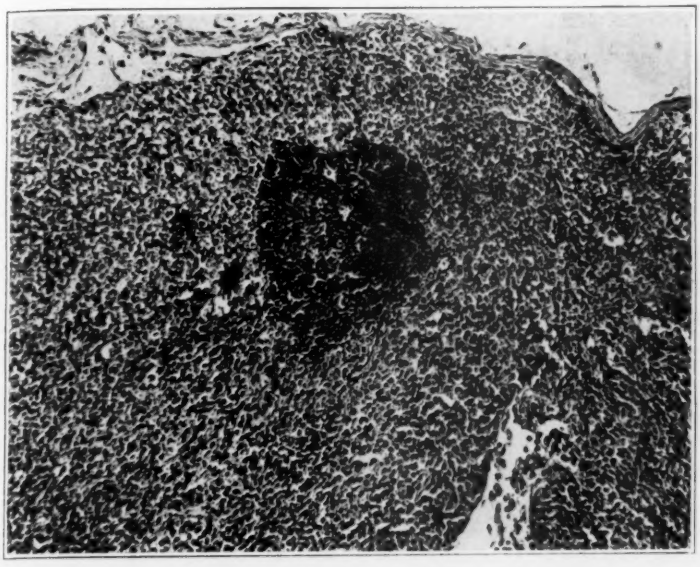

Fig. 3.—Section of lymph node showing replacement of cortex by reticulo-endothelial proliferation. Only a small island of normal lymphoid tissue remains.

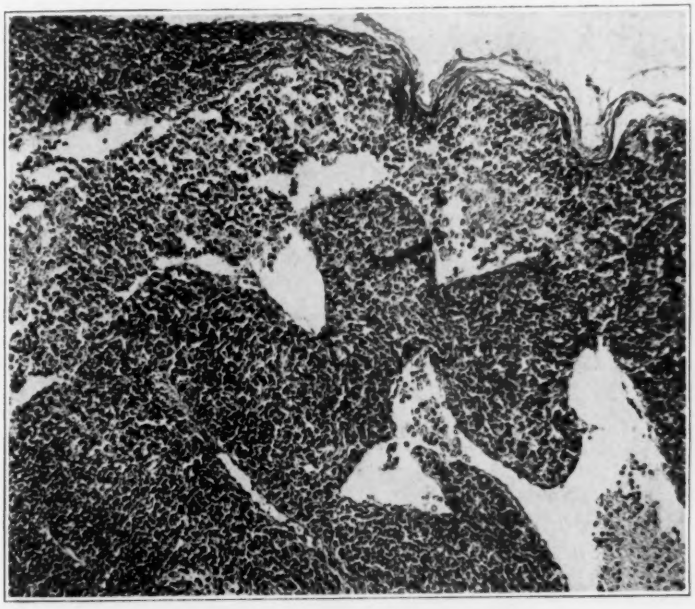

Fig. 4.—Section of lymph node showing cortical sinus crowded with monocytes. The reticulum between sinuses is expanded by proliferation into broad trabeculae.

question as to the identification as monocytes and macrophages, from which there was a clearcut transition to fixed Kupffer cells. There were large numbers of monocytes in some of the dilated portal veins, but in view of a large intermixture of hemosiderin granules it was considered possible that their presence was artefact, i. e., due to postmortem "embolism" from the spleen.

Lymph Nodes: In all the sections from the various regional lymph nodes the order of change was the same, consisting of a more or less diffuse reticulo-endothelial hyperplasia. In most sections monocytes dominated the picture. At times both the reticular and the monocytic features were exhibited in the same histologic section.

In the earlier stages of hyperplasia it was still possible to recognize the architecture of lymph nodes; thus, although the cortex may have been transformed into a broad, diffuse sheet of monocytes, the shadowy outlines of the cortical follicles could still be distinguished. In addition, the lymph sinuses could be clearly discerned; they were filled with monocytes and granular débris. Such positions were particularly valuable for differentiating against a sarcomatous process because the endothelial lining was so frequently preserved over long stretches, even though the ordinarily delicate strand of stroma between them had been transformed into heavy trabeculae as the result of the monocytic hyperplasia. In short, it is believed that if the process had been sarcomatous the normal architecture would have been disrupted in the presence of such a high grade of cellular hyperplasia. One of the peribronchial lymph nodes was of hemolymph type throughout, and in another node of unknown regional origin there was a definite island of such tissue within the capsule.

In other nodes the architecture was completely destroyed. There was a delicate reticular fibrillar stroma, on which the cells were largely spindle shaped or stellate, although smaller or larger areas of free monocytes were interspersed from place to place. It appears thus that monocytes dominated the picture at the earlier and reticulocytes predominated in the later stages of the disease.

As to cytologic details, the cytoplasm was uniformly larger than that of the lymphoid cell; it stained a light basophilic hue with azure II and eosin and at times exhibited dendritic polar processes, which could be followed up into close relationship to reticular fibrillae, as demonstrated by the Mallory aniline blue stain. Where the cytoplasm was relatively bulky it was finely vacuolated, and some cells contained granular débris and fragments of erythrocytes, which indicated phagocytic properties. Their nuclei were larger and more vesicular than those of lymphocytes and had a clearcut perinuclear membrane and a delicate spongy chromatin structure. Nucleoli were often absent or ill defined, although some cells contained from one to three distinct small round to stellate chromatin bodies. Mitotic figures averaged 2 per high power field; many nuclei were indented, and some were folded; the latter variations from the usual round to oval shapes were noted especially in the loosely arranged, relatively free cells. A definite genetic relationship between cells within the sinus and those lining it was established; the phagocytic quality of the cells was best demonstrated within sinuses. These cytologic studies were particularly valuable in differentiating the condition from Hodgkin's or Sternberg's disease because the proliferating cell types were so pure, i. e., reticular and sinus endothelial cells.

Spleen: The large nodule which occurred in this organ had the same structure as that described for the lymph nodes, i. e., the normal architecture was destroyed except for persisting trabeculae and an occasional shadowy splenic nodule or sinus. There was a tendency toward early stages of sclerosis. In parts of the spleen not involved by the nodule the general architecture was still fairly well

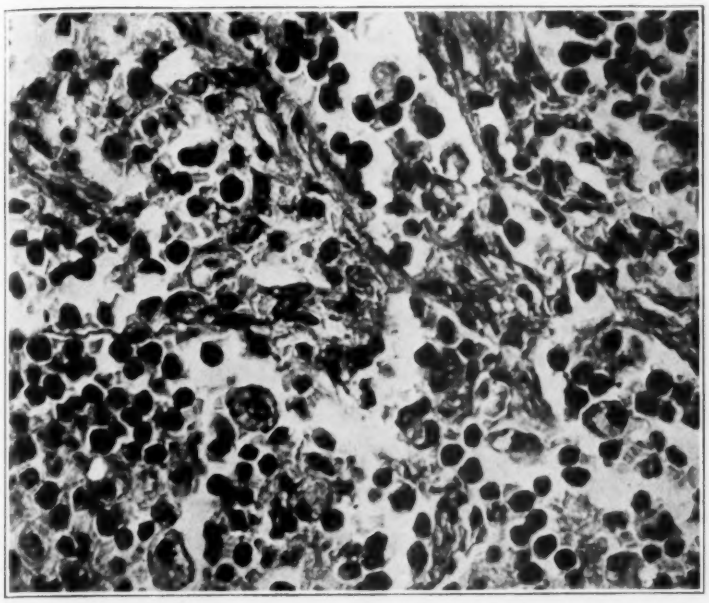

Fig. 5.—Section of lymph node showing monocytes and macrophages in sinuses.

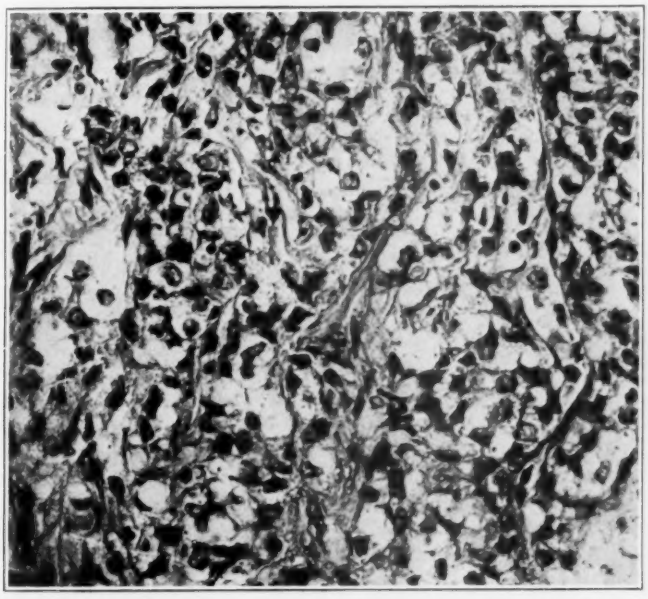

Fig. 6.—Section of lymph node showing marked reticulo-endothelial hyperplasia.

preserved. However, the splenic nodes were poor in cells, and the sinusoids were crowded with monocytes and endothelial cells. Here again transition between cells of the reticulum and those of the sinuses was clearcut.

Bone: The periosteum was massively thickened or replaced by diffuse infiltrations of monocytes and reticular cells. The marrow spaces were hugely dilated by the same types of cell. Hematopoietic cells could not be identified, being replaced by a loose fibrillar stroma supporting irregular accumulations of the monocytic cells. The cortex of the bone was partially destroyed, scattered remnants of broken-down trabeculae remaining in the degenerated masses of cells. The subcortical cancellous bone was sparsely trabeculated, the trabeculae being rather bulky and occasionally exhibiting zones of proliferating osteoblasts at their borders.

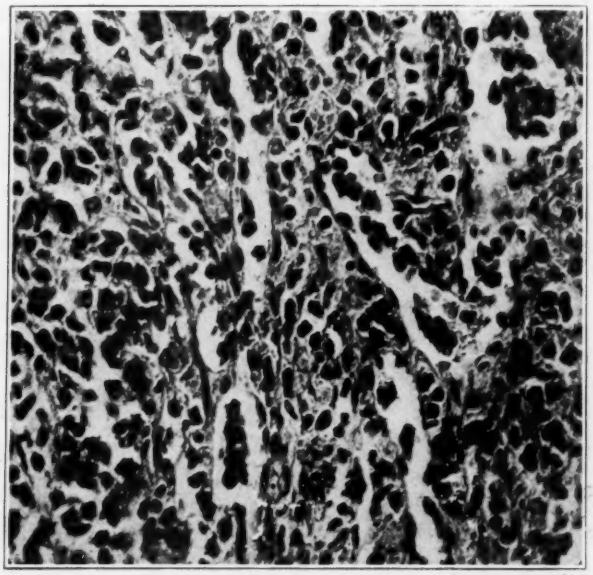

Fig. 7.—Section of spleen showing hyperplasia of sinus endothelium as well as of cells of the reticulum similar to the changes in the lymph node.

Skin: The epiderm was essentially normal. In the corium the heaviest infiltrations occurred in the deepest parts. They were essentially diffuse, the only suggestions of localization occurring around the hair follicles. At one place the tissue consisted entirely of broad areas of infiltrating cells within which a few islands of collagenous material were enclosed. In positions less extensively involved the cells occurred as chains which surrounded the collagen bundles so uniformly as to produce a mosaic appearance. In other parts there was a definite tendency for such closely placed strands to extend parallel to the cutaneous surface.

As to the type of cell concerned, monocytes predominated, being most conspicuous in the more massive infiltrates of the deeper parts of the corium and subcutaneous tissue. The reticular arrangements also occurred in masses, and it was in these that the aforementioned parallel strands occurred.

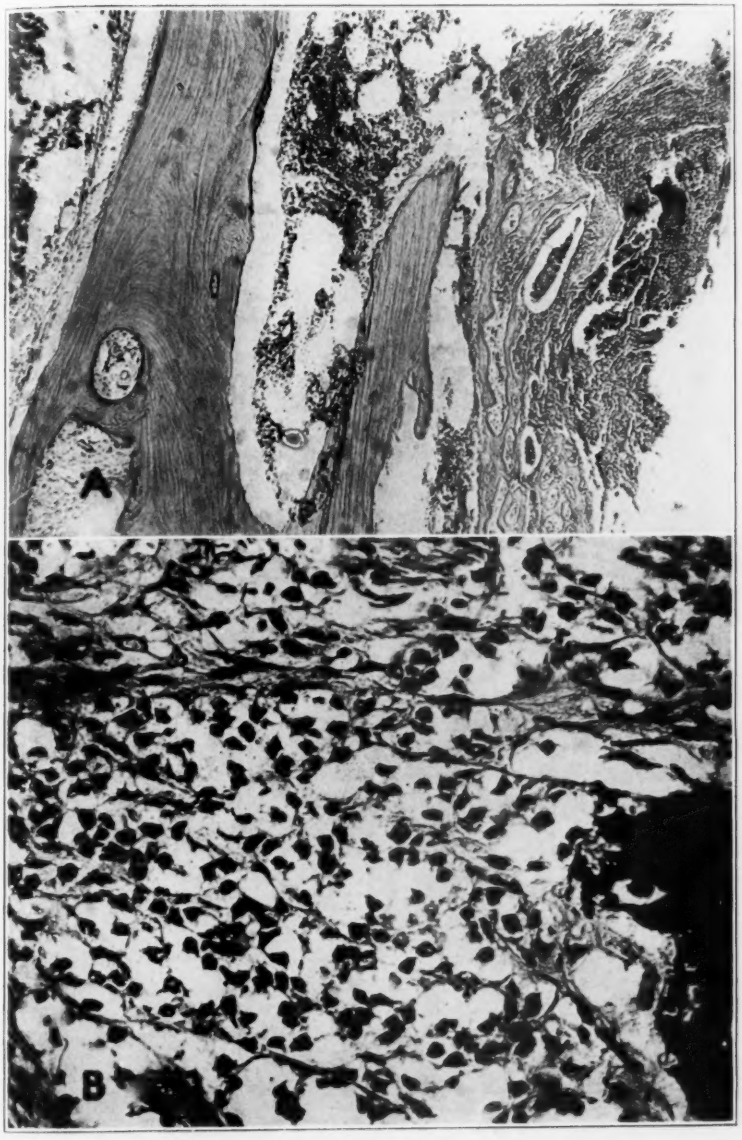

Fig. 8.—*A*, section of bone marrow showing replacement of normal hematopoietic tissue by monocytes. Marked cortical thinning and erosion and infiltration of the periosteum were present but are not visible in the section. *B*, section of bone marrow showing reticulosis.

The uppermost parts of the corium, while notably infiltrated, were inconspicuous in this respect in comparison to the deeper parts. The pars papillaris was not involved. In the subpapillary region the cells approached more the size of the lymphocyte, although larger monocytic cells were frequently identified as such, particularly when they occurred as more or less cylindric masses in the lymph spaces.

There was one mass of sharply circumscribed cells, measuring 10 by 4 mm., which was so sharply separated from the skin proper that it clearly indicated an independent subcutaneous nodule. In sections studied it did not appear to have any connection with the dermal infiltrate.

Summary of Histologic Observations.—The most massive involvement occurred in the lymph nodes, skin, bone marrow and spleen. The order of change was

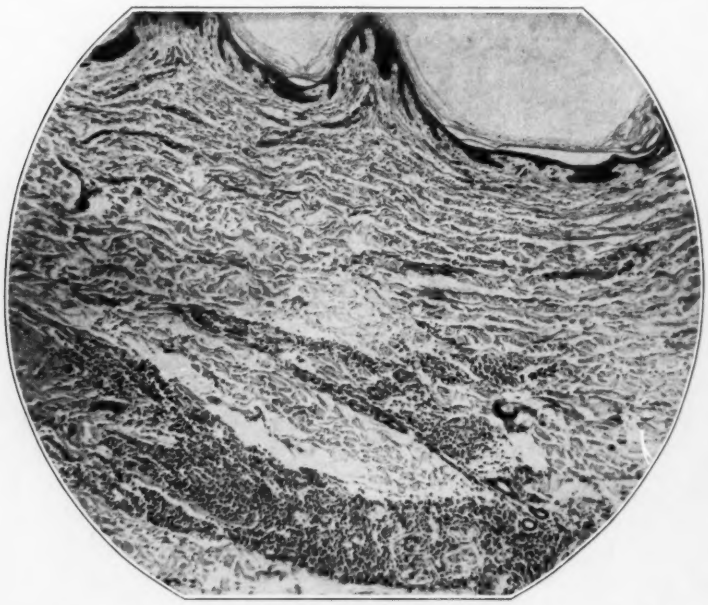

Fig. 9.—Section showing location of infiltration deep in the skin.

the same in all, consisting of such extensive infiltrations of monocytes and stellate and spindle cells that the normal architecture was greatly destroyed. The affinities of such cells were established, we believe, with the reticulo-endothelial system (1) because blood-forming tissues were the ones outstandingly affected and (2) because the types of cells concerned could be referred to that system by appropriate staining methods. In the latter connection phenomena observed in the spleen and liver were of particular value because they established relationships between fixed cells of reticulo-endothelium and the free ones in the sinuses.

Histologic Diagnosis.—The diagnosis based on histologic observations was diffuse reticulo-endotheliosis affecting the lymph nodes, spleen, bone marrow, liver and skin and fibrocaseous tuberculosis of the lungs.

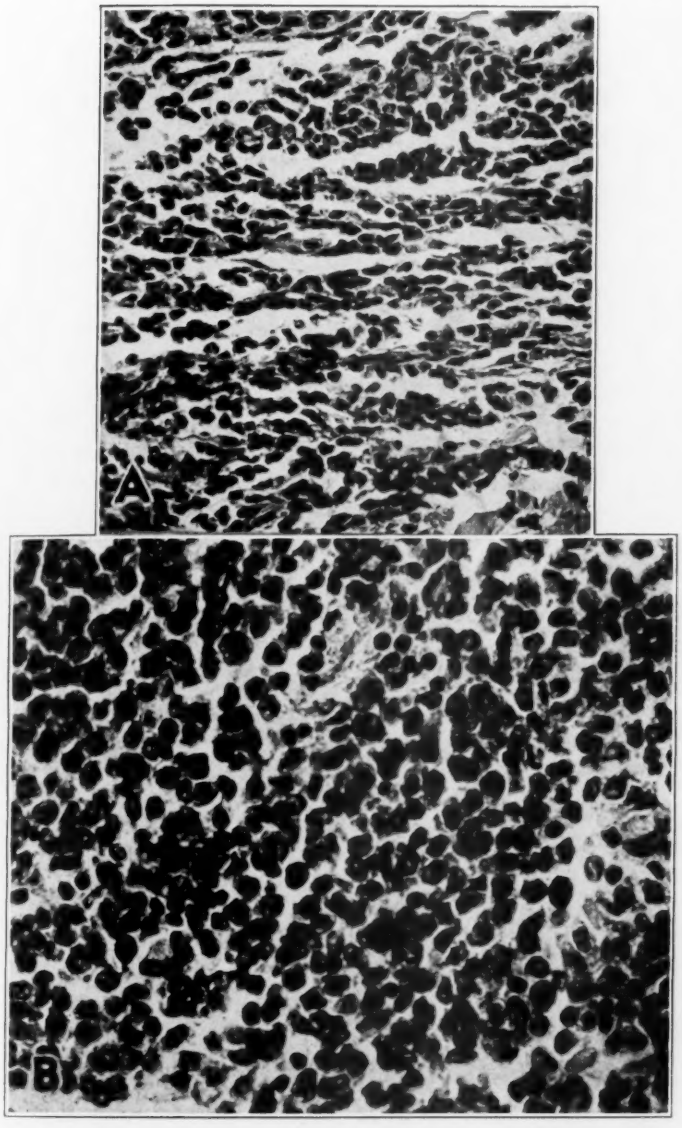

Fig. 10.—Section of skin showing (*A*) reticular type of infiltration and (*B*) free monocytic type of infiltration.

CLASSIFICATION

In the beginning, Warthin included thirty-two cases of granuloma fungoides among his five hundred and six cases of lymphoblastoma. He classified the disorder as follows:

	No. of Cases
Aleukemic lymphoblastoma	23
Aleukemic lymphoblastoma becoming leukemic	5
Aleukemic myeloblastoma	1
Leukemia cutis	3

This is sufficient to indicate that it was his intention to classify certain types of lymphoblastoma when they occurred on the skin with the clinical entity known as granuloma fungoides. He regarded all the lymphoblastomas as neoplastic; subsequently this thesis has been criticized (Ewing,[8] Krumbhaar[10]), but it is not within the purview of this paper to enter into the interminable ramifications involved in the classification. Suffice it to say that as things stand today the general term cutaneous lymphoblastoma has become established among dermatologists as a convenient clinical designation to cover granuloma fungoides-like entities up to the point where more exhaustive studies become sufficient to indicate some definite relationship of the cutaneous condition to internal body processes. That is, we believe that the term cutaneous lymphoblastoma by virtue of usage is a useful, although only temporary, designation and that it should be retained until "cell type" nomenclature becomes stabilized. It should not connote any particular pathologic process. Just as soon, however, as a particular disorder can be classified according to a particular involvement of blood-forming tissue the term should be replaced by a more accurate one couched in terms of hemocytology.

A rather complete catalog of such conditions has been compiled.[11] Suffice it to say for the present that theoretically there are twenty-two such disorders, of which thirteen have been thus far recorded which exhibit cutaneous expressions of one kind or another. Some of the thirteen disorders have been recorded but once or twice; the ones most commonly met are already well known to dermatologists, namely, Hodgkin's disease, granuloma fungoides, leukemic lymphadenosis and aleukemic lymphadenosis. In how far the cutaneous features can be

8. Ewing, James, cited by Krumbhaar.[10]

9. Footnote deleted by author.

10. Krumbhaar, E. B.: The Lymphomatoid Diseases, J. A. M. A. **106**:286 (Jan. 25) 1936.

11. Weidman, Fred D., and Custer, R. P.: The Scope of the So-Called "Cutaneous Lymphoblastomas" in Relation to Lesions of the Haematopoietic System, Proc. Internat. Dermat. Cong. **2**:91 (Sept.) 1935.

reconciled with granuloma fungoides remains to be ascertained. But in any event it must be admitted that it is constructive to add other diseases to the list even though they occur rarely.

Differential Diagnosis.—In our case Hodgkin's disease may be eliminated not so much on clinical as on histologic grounds. While the degree of fibrosis was suggestive, Dorothy Reed cells were not observed. The purity of the cell type already mentioned is decisive. Reticulum cell sarcoma (including Hodgkin's sarcoma) may be similarly eliminated because in the extensive examinations of tissue the histologic picture of that condition was not observed.

Lymphosarcoma and leukosarcoma may be eliminated because a primary focus did not exist; again, the precise cytologic studies already emphasized remove these possibilities. As to granuloma fungoides, we have already indicated that we have no objection to this designation so far as the cutaneous aspects are concerned; we prefer to go farther, however, and aim at a diagnosis which will connote the entire biologic situation.

COMMENT

In our case there was a preliminary itchy diffuse dermatitis lasting five months; after a remission resulting from treatment it recurred in a modified form in four months. Symptoms of pulmonary tuberculosis were recognized at the eleventh month. At the twelfth month a nonpruritic dermatitis developed. At the thirteenth month a moderate adenopathy and splenomegaly were detected. The tumor stage developed at the thirteenth month, after which the remaining course of the disease (nine weeks) was fulminating, consisting of marked emaciation, fever, severe symptoms in the joints and death.

The roentgen studies were valuable in that they demonstrated disease in the bone marrow with infiltration and destruction of bone—a point which may be of some diagnostic value in cases of similar disorders in the future. These observations were confirmed at necropsy, after which microscopic examination of tissue referred the proliferative processes to the reticulo-endothelial system. Since there was no leukocytosis at any time, the disorder may be classified as an aleukemic reticulosis.

With two important exceptions this disorder closely parallels the leukemic reticulosis (monocytic leukemia) studied by Mercer and by Loveman—the clinical course was rapidly fatal, the adenopathy was not extreme and the cytologic picture was similar. It may be of significance as pointing to the reticulo-endothelial system that the lesions were dusky or bluish red; this remains to be determined as a generality. By contrast with leukemic reticulosis, the disorder in our case produced lesions of the order of tumors and did not produce a leukocytosis.

SUMMARY

A widely generalized dermatosis affecting a Filipino in Hawaii passed through a premycotic and a tumor stage. The course was fulminating, covering only fifteen months. At necropsy extensive tumor-like infiltration of all the blood-forming tissues was found. Histologic examination referred the proliferation to the reticulo-endothelial system. As leukocytosis did not occur, the disorder must be regarded as aleukemic reticulosis to which were added cutaneous expressions of the order met in the lymphoblastomas.

Since the cutaneous features were regarded in Hawaii variously as those of leprosy or of Hodgkin's disease and since the cutaneous course paralleled that of the lymphoblastomas, the importance of studies of the lymph nodes and bone marrow are obvious in establishing the diagnosis. It is therefore urged that in future cases of lymphoblastoma biopsies on bone marrow from the sternum be made.

It is evident that in this case aleukemic reticulosis reproduced the clinical symptoms and course of the lymphoblastomas. As the original scope of the lymphoblastomas, as defined, did not clearly include the reticuloses, the condition in our case can be classified with the lymphoblastomas only by sufferance or until it is definitely known that Keim and Warthin intended to assign a wider scope to their concept of lymphoblastoma. In any event, rather than attempt the construction of a new pathologic entity which would accommodate the disorder exhibited by our patient as well as other diseases of blood-forming tissue characterized by the presence of cells of a particular type, we deem it wise to place it tentatively in the group of the lymphoblastomas, or, better, in that of the "lymphomatoid diseases" as defined by Krumbhaar.[10] Dermatologists must await a sufficient accumulation of cases and the results of exhaustive studies of blood-forming tissues with attention to cell types before attempting the final analysis, generalization and classification which would lead to a logical nomenclature for the mycosis fungoides-like dermatoses which are associated with disease of blood-forming tissue. Cases of such disorders cannot be discovered without a searching study of the cell type concerned according to the methods of hemocytologists, in which biopsies on marrow from the sternum as described by Custer [12] promise most help to the clinician.

ABSTRACT OF DISCUSSION

DR. A. B. LOVEMAN, Louisville, Ky.: There is a great deal of controversy concerning the actual existence of monocytic leukemia because of the diversity of opinion regarding the origin of the monocyte. Drs. Wayson, Weidman and

12. Custer, R. P.: Studies on the Structure and Function of Bone Marrow, Am. J. M. Sc. **185**:617 (May) 1933.

Lynch apparently favor the theory of reticulo-endothelial origin at least in part. Monocytic leukemia (Schilling type) may be considered a pathologic condition in which there is extensive hyperplasia of the reticulo-endothelial tissues associated with the appearance in the peripheral blood of abnormal cells of the monocytic series.

The condition of the patient of Dr. Wayson and Dr. Weidman certainly resembled mycosis fungoides clinically. Pathologically there was an extensive reticulosis or reticulo-endotheliosis. The fact that there were no abnormal white cells in the peripheral blood further classifies the disorder as aleukemic reticulosis or aleukemic reticulo-endotheliosis. Had the peripheral blood revealed extensive invasion of immature and abnormal cells of the monocytic series, the condition would have qualified as monocytic leukemia. The invasion of the blood stream by these cells does not alter the fundamental pathologic process. In fact, the authors stated that the condition in their case practically paralleled that in previously reported cases of leukemic reticulosis (monocytic leukemia) with the exceptions that their patient had no changes in the peripheral blood and that cutaneous tumors were present.

One of the most interesting features in this case is the invasion of the osseous tissue. It is quite likely that in the future the recognition of such involvement by roentgen examination may prove to be of great diagnostic significance.

I concur heartily with Drs. Wayson and Weidman in their opinion that both leukemic and aleukemic reticulosis should be admitted to the group of lymphoblastomas.

Dr. Lynch has performed a gigantic task in his attempt to differentiate monocytic leukemia (leukemic reticulosis) from aleukemic reticulosis on clinical and histologic grounds. Heretofore I have regarded such a differentiation as impossible, and I still favor the view that the two conditions are fundamentally the same except that one is associated with extensive abnormality in the peripheral blood whereas the other is not.

Dr. Lynch stated that some authors prefer to consider monocytic leukemia in its aleukemic form and aleukemic reticulo-endotheliosis as the same disease. I do not share this opinion, because aleukemic reticulo-endotheliosis implies, as Dr. Wayson and Dr. Weidman stated, a reticulosis with no appearance of abnormal cells in the blood stream, whereas an aleukemic state of monocytic leukemia implies at least some qualitative changes in the blood, although the white blood cell count may not exceed the normal limit.

There is some doubt in my mind as to the exact classification of the disorder in several of Dr. Lynch's cases. Case 1 is undoubtedly one of reticulosis, but without knowledge of the hematologic data it is difficult to classify it as one of leukemic reticulosis. Two additional cases were reported as examples of aleukemic reticulo-endotheliosis. In the one (case 6) there was an abnormally high white blood cell count with only 10 per cent mature white cells; in the other (case 7) there were 65 per cent atypical mononuclear cells although the total count was only 4,000 white cells per cubic centimeter. In both of these cases there was rather extensive monocytic infiltration of the skin. It is difficult to rule out monocytic leukemia in these cases—in case 7, however, the disorder was in its aleukemic phase.

It is questionable whether the cutaneous manifestations were sufficiently characteristic to be diagnostic or pathognomonic per se. This is well illustrated when one compares the similar pathologic features in the case of Dr. Wayson and Dr. Weidman and those in some of Dr. Lynch's cases and yet observes the great divergence in the cutaneous manifestations. As leukemic and aleukemic reticulosis become better recognized, a diversity of cutaneous manifestations will undoubtedly be noted.

The cutaneous necrosis noted in several cases may well be the result of marked diminution or of absence of polymorphonuclear cells in the blood stream. I have seen similar lesions associated with agranulocytosis, granulocytopenia and aplastic anemia—the diseases, incidentally, which are sometimes difficult to differentiate from the aleukemic phase of monocytic leukemia.

Both of these papers were well presented and should prove thought stimulating to the dermatologist. They show clearly that correlation of the clinical, hematologic and histologic features is necessary to establish a specific diagnosis. Future progress will depend more on the accurate recognition of the cell type than on any other single factor.

Dr. Arthur W. Stillians, Chicago: I wish to mention a case of monocytic leukemia presented before the Chicago Dermatological Society some years ago. The patient at one time had a white blood cell count of 23,000 and from 50 to 71 per cent monocytes. There was a generalized exfoliative condition associated with infiltration of the skin and many distinct, sharply defined papules.

Histologic studies showed no specific infiltration, but, as has been stated, it may be that a specimen taken later would have given different results.

The patient was 70 years old and derived much benefit from roentgen treatment. She died a couple of years later of pneumonia.

Dr. Hamilton Montgomery, Rochester, Minn.: It is important to differentiate between the Naegeli and the Schilling type of monocytic leukemia. In both there is indentation of the nuclei to a certain extent, and the two conditions can be differentiated only by careful hemocytologic studies. I do not believe that they can be differentiated on the basis of the histologic picture in sections of the skin alone. Hemocytologists do not agree regarding the origin of all the white cells. Some maintain that the reticulo-endothelial cells and the monocytes can also give rise to lymphocytes, thus linking the reticulo-endothelial diseases with the lymphoblastomas. I therefore believe that the term lymphoblastoma is as good a one as can be used for the time being.

Two cases of monocytic leukemia of the Naegeli type were observed at the Mayo Clinic. In one of these the disorder started with generalized erythroderma, mycosis fungoides-like plaques and the histopathologic picture of a nonspecific lymphoblastoma. Only after four years, shortly before the patient's death, did the hemocytologic examination give positive results and show a Naegeli type of monocytic leukemia, with 40 per cent monocytes. The condition in this case probably represented the autochthonous development of a lymphoblastoma which in the beginning was mycosis fungoides and terminated as a Naegeli type of leukemia.

In the other case changes in the blood appeared first and cutaneous manifestations consisting of nodules and necrosis developed only in the terminal phases.

Mycosis fungoides, as Fraser has emphasized, is accompanied by marked changes in the reticulo-endothelial cells of the skin, and there may be a certain number of immature monocytes as well as immature forms. It is important to correlate all the various diagnostic measures in order to arrive at a correct diagnosis in cases of monocytic leukemia or of any of the lymphoblastomas.

Dr. D. W. Goldstein, Fort Smith, Ark.: Recently I have observed a case of monocytic leukemia in a woman aged 58 who was referred to me because of a purpuric lesion on the cheek which resembled a streptococcic blister. There was no localized erythema or swelling around the lesion. The patient's temperature was 101 F. There were no palpable glands or enlargement of the spleen. Examination of the oral cavity disclosed an ulcer on the gingival surface at the second bicuspid tooth. This lesion had previously been cauterized. A purpuric lesion

was found on the posterior wall of the pharynx. A blood count showed 88,000 white cells and numerous other cells which were considered to be monocytes. A tentative diagnosis of monocytic leukemia was made. Several days later the total white cell count was 150,000, and there was an increase in the number of monocytes. Ulcerative gingivitis developed during the next few days. There was also an increase of the number of white blood cells and in that of monocytes. The patient was sent to the hospital for transfusion five days after the diagnosis was made, but she died suddenly two hours after entering the hospital. Permission for autopsy was refused. Slides were sent to the Simpson Memorial Institute, Ann Arbor, Mich., where the diagnosis of monocytic leukemia was confirmed.

Dr. M. G. Bohrod, Peoria, Ill.: Dr. Weidman mentioned the necessity for a broader name to include the whole group of diseases under consideration. Evidently unless one believes that the monocyte and the lymphocyte have interrelations and can be formed one from the other, this group of diseases does not belong to the lymphoblastomas; and certainly the name lymphoblastoma cannot be applied to the specific cutaneous lesions associated with the myelogenous types of leukemia.

In pathology the whole group of diseases due to marked proliferation of the cells of the circulating blood and of their precursors does have a name, and I think that this name could be applied to the special manifestations under consideration. Since the whole group of white cells—monocytes, lymphocytes and granulocytes—are called leukocytes, the name given to all these neoplastic or pseudoneoplastic diseases is leukoses. The simple name cutaneous leukoses could be adopted, for the cutaneous manifestations, and that would cover the entire group.

Dr. Fred D. Weidman, Philadelphia: It has been brought out by a number of the discussers that controversy about terminology still runs riot among hematologists. That is one more reason for dermatologists to refrain from trying to adapt dermatologic nomenclature too strictly to hematologic nomenclature. One should let the hematologists fight out the question among themselves. When they have stabilized their nomenclature it will be possible for dermatologists to multiply the dermatologic nomenclature.

The general practicing dermatologist wishes to know how he can help the hematologist in the finer cytologic studies of these conditions. 1. He should take numerous, at least a dozen, samples of blood. The hematologist has to employ various stains. It may be necessary to make the oxidase test and to use Mallory's connective tissue stain and other stains. 2. He should secure a sample of bone marrow, if possible. Dr. Custer has published the technic for securing biopsy material from the bone marrow of the sternum. He does it often at the Philadelphia Hospital, and thus far the procedure has never caused osteomyelitis. 3. The dermatologist should have roentgenograms made. It is obvious that where there is involvement of the marrow and bones, this is a logical avenue to turn to.

In some of Dr. Lynch's cases the disorders were suggestive because they had a bearing on etiology. In the first cases that he reported the disorder started as what appeared to be an infection and the course was fulminating. If these cases are to be accepted as instances of disease of blood-forming tissue—classified as leukemia—it appears that some types of leukemia at least have an acute infectious causation, which is pertinent to the controversy whether the lymphoblastomas are neoplastic or not. Warthin and the Michigan school in general contend emphatically that the lymphoblastomas and Hodgkin's disease are neoplastic conditions.

Dr. Francis W. Lynch, St. Paul, Minn.: Dr. Montgomery mentioned the reticulo-endothelial origin of lymphocytes. Although it was not indicated on the

lantern slide, Downey agrees that some lymphocytes develop directly from reticulo-endothelial cells, but the majority develop in lymphoid tissue by the division of apparently mature lymphocytes.

Dr. Loveman brought up a number of points which deserve comment. First of all, I apparently did not make clear my opinion of the relation between monocytic leukemia and reticulo-endotheliosis. I believe that the Naegeli type of monocytic leukemia must be differentiated from reticulo-endotheliosis and that the two conditions have nothing in common. The Naegeli type of monocytic leukemia is a mixed form of myelogenous leukemia. I think that there are no essential differences between monocytic leukemia of the Schilling type and "primary" reticulo-endotheliosis.

Dr. Loveman rightly questions the classification of the disorder in case 6, in which the white blood cell count was 38,000 and there was a papular eruption on the neck. That is gone into in more detail in the paper. The youth with the chronic ulceration (case 8) presented an interesting blood picture. His white cell counts were within normal limits, but the proportion of the different cells varied considerably. Most often the counts showed that 65 per cent of the cells were lymphocytes, but a few days later as many as 65 per cent would be polymorphonuclear leukocytes; that alternation was repeated several times in the course of the disease.

I am not sure that the understanding of aleukemic leukemia is clear. Is it necessary that qualitative changes in the constituents of the white blood cells be present? May not the white blood cell be entirely normal, showing neither qualitative nor quantitative differences, and yet pathologic changes due to aleukemia be present in the tissues? It is my opinion that this is not uncommon in aleukemic lymphatic leukemia.

CUTANEOUS LESIONS ASSOCIATED WITH MONOCYTIC LEUKEMIA AND RETICULO-ENDOTHELIOSIS

FRANCIS W. LYNCH
ST. PAUL

Since the general knowledge of lymphatic and myelogenous leukemia was greatly advanced by a study of the cutaneous lesions of these conditions, it is unfortunate that dermatologists have only recently become interested in monocytic leukemia. This condition was first described in 1913 by Reschad and Schilling-Torgau,[1] who reported a case of this disease involving the skin observed in Arning's clinic. Monocytic leukemia is characterized by an increase of monocytes in the blood but is indistinguishable clinically from the other leukemias. Both specific and nonspecific cutaneous lesions are commonly associated with this disease.

Reticulo-endotheliosis has also been the subject of much study by hematologists, but the recent advances in the hematologic aspect of this condition have not received sufficient attention in dermatologic literature. Among dermatologists there has developed a tendency to place all atypical pathologic processes involving the hematopoietic and lymphatic tissues in a large ill defined group and to call them all lymphoblastoma.

When Mallory in 1914 introduced the term lymphoblastoma he referred only to the diseases involving tissues and cells of lymphoid nature. Myeloid and monocytic leukemia, reticulo-endotheliosis and established mycosis fungoides should not be included under this title until more definite knowledge as to the development of the various blood and tissue cells is available.

It has been my privilege to observe a number of cases of monocytic leukemia and reticulo-endotheliosis in the various services at the University Hospitals. I shall discuss the clinical and the microscopic manifestations observed in these cases and attempt to show the relationship between these conditions and the other better known diseases of the hematopoietic system. It is hoped that the differentiations will be of

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From the Division of Dermatology, University of Minnesota, Dr. H. E. Michelson, Director.

Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936.

1. Reschad, H., and Schilling-Torgau, V.: Ueber eine neue Leukämie durch echte Uebergangsformen und ihre Bedeutung für die Selbstständigkeit dieser Zellen, München. med. Wchnschr. **60**:1981, 1913.

service to dermatologists in assisting them to diagnose conditions belonging to this confusing group of cutaneous diseases.

I shall not review the older theories of the development of blood cells as propounded by Maximov and by Naegeli. These theories have been modified more recently, but they are still not acceptable to a large group of hematologists. All agree that the mesenchymal syncytium in embryonal life gives rise to all the various blood cells. Downey [2] and many other hematologists believe that cells of the reticulo-endothelial system, which are direct descendants of this syncytium, retain their hematopoietic ability, which may later become manifest in a leukemic state by producing cells of the lymphoid, myeloid or monocytic series. Normally, however, the reticulo-endothelial system is active chiefly in the production of monocytes. Lymphocytes develop in lymphoid tissues almost exclusively by the division of apparently mature lymphocytes, while polymorphonuclear granulocytes develop from immature cells of the myeloblastic series in myeloid tissue.

Monocytes observed in leukemic blood may develop in either of two ways: (1) directly from the reticulo-endothelial system in a manner related to the normal or (2) in myeloid tissue as a development from the myeloblast. Thus two distinct types of monocytic leukemia have been described. In the first there is reticulo-endothelial hyperplasia with mobilization of the cells into the blood and differentiation to monocytes (Schilling type). In the second type the pathologic picture in the tissues is that of myelogenous leukemia, while myeloblasts and other immature granulocytes as well as immature and mature monocytes are present in the blood (Naegeli type).

MONOCYTIC LEUKEMIA

Monocytic leukemia is characterized by an increase in the number of monocytes of the blood. These cells are always present in normal blood but are much less numerous than lymphocytes or granulocytes. They are larger than large lymphocytes and have an abundant weakly basophilic cytoplasm, which is usually granular and frequently vacuolated. The eccentric nucleus is large and vesicular and may be oval, notched or lobulated. As mentioned previously, the monocytes of normal blood are produced by the reticulo-endothelial system. In true monocytic leukemia (Schilling type) the abnormal increase of immature monocytes results from an exaggeration of the normal process; that is, the immature cells are produced by the reticulo-endothelial system.

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2. Downey, H.: Monocytic Leukemia and Leukemic Reticulo-Endotheliosis, in Bell, E. T.: Textbook of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1934; personal communication to the author. Stasney, J., and Downey, H.: Subacute Lymphatic Leukemia, Am. J. Path. **11**:113 (Jan.) 1935.

The first patient reported to have monocytic leukemia [1] presented himself at Arning's clinic with a generalized macular eruption associated with stomatitis and nasal hemorrhages. The cutaneous changes consisted of infiltration with large mononuclear white blood cells. A great excess of monocytes was present in the blood.

Of the manifestations of monocytic leukemia, ulcerative gingivitis, petechiae and subcutaneous hemorrhages are the most common findings of interest to dermatologists. Of a series of cases reported by Doan and Wiseman [3] cutaneous lesions were observed in about half.

Mercer [4] in 1935 reviewed the literature on monocytic leukemia and reported two cases in which the cutaneous eruption was a prominent

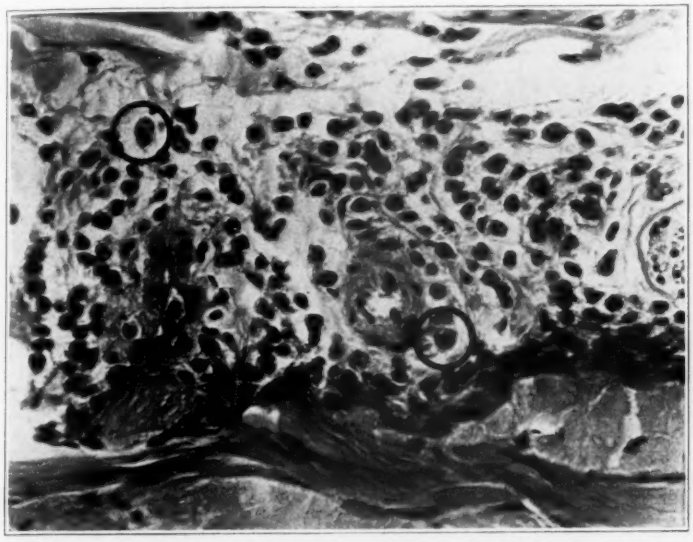

Fig. 1 (case 1).—Section from an early lesion of monocytic leukemia cutis, showing lymphoid and monocytoid infiltration. Only two monocytes are pointed out but many more are present.

feature. He pointed out that two types of specific lesions are met: (1) red or brown macules and papules, which usually become blue later, and (2) pale shotty papules lying deeper in the skin; these lesions may develop into larger nodules.

Loveman [5] has recently reported a case of monocytic leukemia in which specific cutaneous lesions were present. His description of the

3. Doan, C. A., and Wiseman, B.: The Monocyte, Monocytosis and Monocytic Leukosis, Ann. Int. Med. **8**:383 (Oct.) 1934.

4. Mercer, S. T.: The Dermatosis of Monocytic Leukemia, Arch. Dermat. & Syph. **31**:615 (May) 1935.

5. Loveman, A. B.: Monocytic Leukemia Cutis, South. M. J. **29**:357 (April) 1936.

histologic observations is particularly valuable and will be discussed later.

Two further cases of monocytic leukemia with specific lesions are reported briefly.

CASE 1.—In a 67 year old man a penile lesion developed as a result of a chemical burn. Ulceration was followed by painful enlargement of the shaft and glans associated with weakness, chills and fever. Necrotic ulceration of the glans progressed in spite of local therapy. Numerous petechiae as large as 2 cm. in diameter appeared over the entire body. There was also subconjunctival hemorrhage. A febrile course terminated with death five weeks after the onset of the initial symptoms. Microscopic study of the viscera at autopsy showed diffuse monocytic infiltration, sustaining a diagnosis of monocytic leukemia.

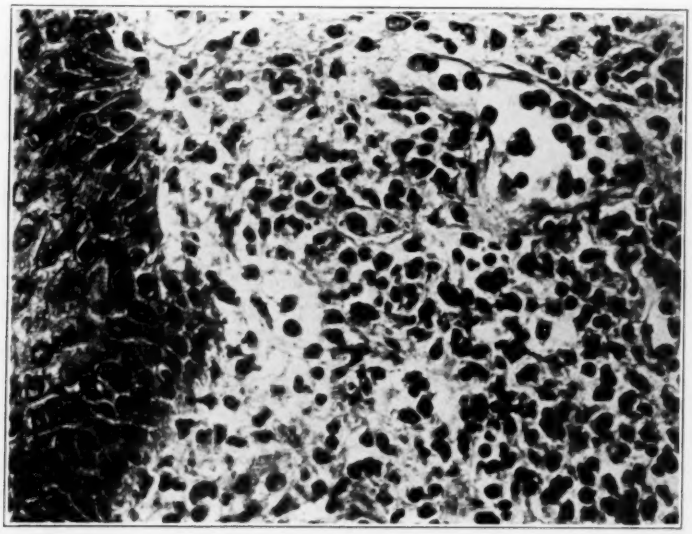

Fig. 2. (case 1).—Section showing a later stage of the disease. There are looser structure, large reticular cells and numerous mature and immature monocytes characteristic of monocytic leukemia cutis.

In tissue removed before death a nonspecific change consisting of polymorphous infiltration and a loose supporting tissue was observed (fig. 1). Sections of tissue removed at autopsy showed many polymorphonuclear leukocytes near the necrotic areas and a few large cells having a clear cytoplasm and a small dark eccentric nucleus. In the areas of diffuse infiltration there were mononuclear cells of various sizes; the smaller cells had round nuclei while the nuclei of many of the larger cells were oval (fig. 2).

This case furnishes an example of the usual course, which progresses rapidly and simulates that of sepsis; even when the disease follows a more chronic course it usually terminates with similar acute symptoms.

The massive infiltration of the genitalia with progressive necrotic ulceration observed in this patient has not previously been described in association with monocytic leukemia.

Naegeli Type of Monocytic Leukemia.—As mentioned earlier, Naegeli has described a type of monocytic leukemia in which immature cells of both the myeloid and the monocytic series are observed. It is Downey's opinion that this disorder represents a form of myelogenous leukemia with hyperplasia of the myeloid tissues in which the myeloblast produces both granulocytes and monocytes.

In one of Montgomery's [6] patients with the Naegeli type of monocytic leukemia the early cutaneous manifestations simulated mycosis fungoides.

CASE 2.—A 58 year old woman had a white blood cell count of 144,000 and immaturity in all lines of polymorphonuclear cells. The diagnosis was mixed leukemia of the chronic monocytic myelogenous type. There were a number of noninflammatory infiltrated lesions on the arms and buttocks and an area of involvement on the leg which may have represented thrombophlebitis. At autopsy a diagnosis of chronic monocytic leukemia was made, but later microscopic study showed myeloid leukemic infiltration of the liver, spleen, kidneys and adrenal glands, and a final diagnosis of chronic myelogenous leukemia was made.

The upper portion of the cutis of an infiltrated lesion was practically free from the cellular infiltration which was rather uniformly diffuse throughout the remaining portions of the cutis. At the lower border were many immature cells; the proportion of lymphocytes increased near the surface of the skin. Many of the immature cells had oval or reniform nuclei, but most of the nuclei were round and slightly larger than those of the lymphocytes; the cytoplasm was eosinophilic and varied in amount.

The condition in case 2 represents the Naegeli type of leukemia and illustrates the difficulty encountered in properly classifying this disease. The cutaneous lesions were not particularly helpful in differentiating between the various types of leukemia, except that the presence of immature eosinophils suggested myelogenous leukemia; immature monocytes were also observed.

LEUKEMIC RETICULO-ENDOTHELIOSIS (EWALD)

In a small group of cases of leukemia one may demonstrate in the smears of blood unusual cells which resemble not only monocytes but also lymphocytes, myeloblasts, plasma cells and reticulo-endothelial cells.[2] Ewald described such a disorder as an instance of leukemic reticulo-endotheliosis; this nomenclature is unfortunate because many writers speak of monocytic leukemia as leukemic reticulo-endotheliosis. The exact relationship between these two diseases is not known.

6. Montgomery, H.: Personal communication to the author.

In contrast with the observations in monocytic leukemia smears of blood from patients with Ewald's leukemic reticulo-endotheliosis show cells more primitive than the myeloblast. There is primary reticulo-endothelial hyperplasia plus increased hematopoietic function; the presence of immature monocytes differentiates this condition from the hyperplasia associated with sepsis which liberates only unaltered reticulo-endothelial cells or histiocytes. Leukemic reticulo-endotheliosis of the Ewald type is not common. It is regarded by some observers as a subleukemic form of monocytic leukemia.

The cutaneous changes observed in the following cases were non-specific and represent merely the hemorrhagic tendency so characteristic of all forms of leukemia. This feature, which is sometimes used as a differential point in distinguishing clinically between leukemia and lymphogranulomatosis, may provide some justification for grouping leukemic reticulo-endotheliosis with the true leukemias.

CASE 3.—A 66 year old man exhibited the clinical and hematologic picture of chronic leukemic reticulo-endotheliosis. There were a number of petechiae in the scapular and clavicular regions and ecchymoses on the extremities. No other cutaneous lesions were observed. After four transfusions of blood the purpuric tendency disappeared.

CASE 4.—A 51 year old man had the hematologic picture of leukemic reticulo-endotheliosis, with the reticular cells differentiated toward lymphocytes. He presented scattered petechiae, and later evidence of subcutaneous hemorrhages appeared on the trunk and extremities. There was also hemorrhage from the nose and mouth associated with a severe anemia.

Microscopic examination of one of the petechial areas did not show any change in the capillaries but disclosed only extravasation of red blood cells. There were no specific changes in the perivascular tissues.

ALEUKEMIC RETICULO-ENDOTHELIOSIS

The term reticulo-endothelial system has been used loosely to include nearly all the connective tissues of the body. Used in a strict sense it refers to the reticulum cells of the spleen and other lymphoid tissue as well as to the reticulo-endothelial cells of the lymph sinuses of the nodes and the blood sinuses of the spleen, liver, bone marrow, adrenal cortex and hypophysis. This system is composed of large mononuclear vacuolated cells capable of taking up granular material for storage.

Hyperplasia of the reticulo-endothelial system is a common response to infection and is evidence of the relation of this system to the development of immunity. In banal acute infections there is often sufficient response of this system to produce an increase of monocytes in the blood; occasionally in acute sepsis there is such active reticulo-endothelial response that unaltered reticulo-endothelial cells may be liberated into the blood stream. These observations correspond to the liberation into the blood stream of immature lymphocytes or granulocytes which frequently occurs in acute septic conditions.

Reticulo-endothelial hyperplasia is observed in certain chronic infectious diseases and in lymphogranulomatosis, granuloma fungoides and sarcoma of Kaposi. There is frequently an increase of monocytes in the blood and tissues in these diseases. The reticulo-endothelial system may also be involved in a lymphosarcomatous process, as pointed out by Fraser and Schwartz,[7] who classified reticulo-endothelial disease with the lymphoblastomas because they believed that ". . . the most constant anatomic function of the primitive reticular cells . . . is the production of the lymphatic series of cells." Observers who believe that the reticulo-endothelial cell is more active in producing monocytes than lymphocytes cannot place reticulo-endotheliosis with the lymphoblastomas as defined by Mallory.

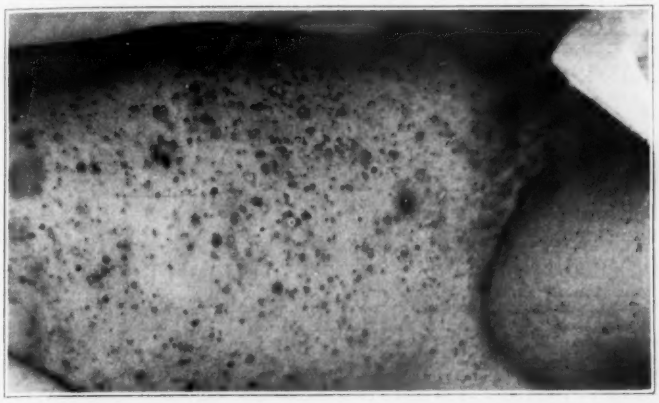

Fig. 3 (case 5).—Generalized pustular eruption in an infant who died of acute reticulo-endotheliosis. The lesions were specific.

Hyperplasia of the reticulo-endothelial system associated with acute or chronic infectious processes or with the aforementioned granulomatous conditions is occasionally referred to as reticulo-endotheliosis. One must recognize that such reticulo-endothelial hyperplasia is secondary to the other process just as myeloid or lymphoid hyperplasia may be observed secondary to other diseases.

In lymphatic and myelogenous leukemia the hyperplasia of the lymphoid or myeloid tissue respectively is the essential feature of the disease, and aleukemic phases are observed with no changes demonstrable in smears of the blood. Since the hematopoietic tissue for monocytes consists chiefly of the reticulo-endothelial system, hyperplasia of this system should be the most striking feature of aleukemic monocytic leukemia. Because many confusing pathologic changes are observed in the reticulo-endothelial system and their exact relationships are not

7. Fraser, J. F., and Schwartz, H. J.: Neoplastic Disease of the Reticulo-Endothelial System, Arch. Dermat. & Syph. **33**:1 (Jan.) 1936.

absolutely known this condition is at present described as "reticulo-endotheliosis," although many observers regard it as the aleukemic manifestation of monocytic leukemia.

Aleukemic reticulo-endotheliosis may be acute [8] or chronic.[9] The clinical course of the acute form is characterized by sudden onset, fever, necrotic angina and hemorrhagic diathesis—features which correspond to those of the other forms of acute leukemia and which recall Sternberg's opinion that acute leukemia is the result of sepsis. Although bacterial organisms have been observed in a few cases, in the majority they cannot be demonstrated, and most observers regard their presence as evidence of secondary invasion.

Chronic aleukemic reticulo-endothelial proliferation may be difficult to distinguish clinically and pathologically from the hyperplasia secondary to chronic infectious processes or lymphogranulomatosis; atypical forms may present a most confusing symptomatology and pathology. In spite of confusion as to the proper interpretation of the observations in some cases of these disorders there remains a group which most competent observers regard as chronic aleukemic reticulo-endotheliosis and which may well be called aleukemic monocytic leukemia.

The cutaneous lesions of reticulo-endotheliosis do not differ greatly from those of leukemia. In the acute forms one may observe macular or papular eruptions which seldom lead to the development of deeper nodules. There is a tendency to hemorrhage or necrosis in these lesions, and distinctly pustular eruptions may be observed, such as occurred in case 5.

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9. Goldschmid, E., and Isaac, S.: Endothelhyperplasie als System-Erkrankung des hämatopoetischen Apparates, Deutsches Arch. f. klin. Med. **138**:291, 1922. Tschistowitsch, T., and Bykowa, O.: Retikulose als eine Systemerkrankung der blutbildenen Organe, Virchows Arch. f. path. Anat. **267**:91, 1928. Géry, L.; Wolf, M., and Grévillod: Réticulo-granulomatoses, Am. J. Cancer **22**:243, 1934. Lauritzen, K.: Ein Fall einer systemartigen Retikulumzellhyperplasie, Virchows Arch. f. path. Anat. **279**:603, 1931. Flarer, F.: Cutaneous Endothelioma with Systemic Manifestations, Arch. Dermat. & Syph. **31**:95 (Jan.) 1935; Zentralbl. f. Haut- u. Geschlechtskr. **49**:154, 1934.

CASE 5.—An eruption on the buttocks was noticed when the patient was 4 months old (fig. 3). The lesions were macular and then became vesicular; they were followed by others appearing in the same region and then on the scalp, trunk and proximal portions of the extremities. Two months later there was a generalized pustular eruption. The white blood cell count was 15,000, and the differential count was normal. An infection of the middle ear developed, and the cutaneous lesions became more severe, consisting of oval crusted shallow ulcers 0.5 cm. in diameter. There were numerous petechiae. Study of the nodes, liver and spleen at autopsy showed reticulo-endothelial proliferation; this led to a diagnosis of aleukemic reticulo-endotheliosis.

In the early lesions there was a loss of the epidermis near the follicle with lymphocytic infiltration around the follicle and the sweat glands. Some large pale cells in the background were not noted at the first examination, and the disorder was regarded as pyoderma. At the borders of the more advanced lesions there was perivascular infiltration with polymorphonuclear cells, small lymphocytes and some larger mononuclear cells. The main portion of the lesion had a loose fibrillary structure with dilated capillaries and some nonspecific infiltration; the predominant cell was larger, round or oval and had a clear cytoplasm; from some of these cells narrow processes extended into the fibrillary tissue. The nuclei were pale, and many were reniform or bilobed (figs. 4 and 5).

Chronic aleukemic reticulo-endotheliosis with cutaneous changes has been reported by a number of observers. There seems to be nothing characteristic about the macular, papular and nodular eruptions which have been described; the hemorrhagic tendency is not so evident as in the acute forms. Other clinical features are also nonspecific: there are usually general weakness, fever, anorexia and loss of weight. The liver, spleen and lymph nodes may be enlarged. In cases of this as in those of the acute condition the diagnosis is usually not made until there is opportunity to examine the tissues microscopically.

Case 6 is reported as an example of chronic reticulo-endotheliosis because of the final pathologic observations. The condition is representative of the large group of disorders in which the clinical, hematologic and pathologic processes at various times resemble various diseases. Many observers classify such a disorder as a nonspecific lymphoblastoma.

CASE 6.—A 38 year old woman suffered from weakness and menorrhagia, resulting in severe anemia. Examination of the blood showed that only 10 per cent of the white cells were mature; the count was 38,000. A tentative hematologic diagnosis of acute myeloblastic or stem cell leukemia was made. There were petechiae on the conjunctivae and hemorrhagic areas on the uvula and buccal mucosa; retinoscopic examination showed petechiae and hemorrhagic areas. An eruption on the posterior surface of the neck (fig. 6) consisted of a large number of elevated disklike nodes which acquired an increasingly deep blue color. On the legs and arms were tender deep-seated red nodules resembling those of erythema nodosum.

Sections of the papules showed an edematous fibrillary cutis with only a few small lymphocytes and a few larger cells having small dense nuclei or two or

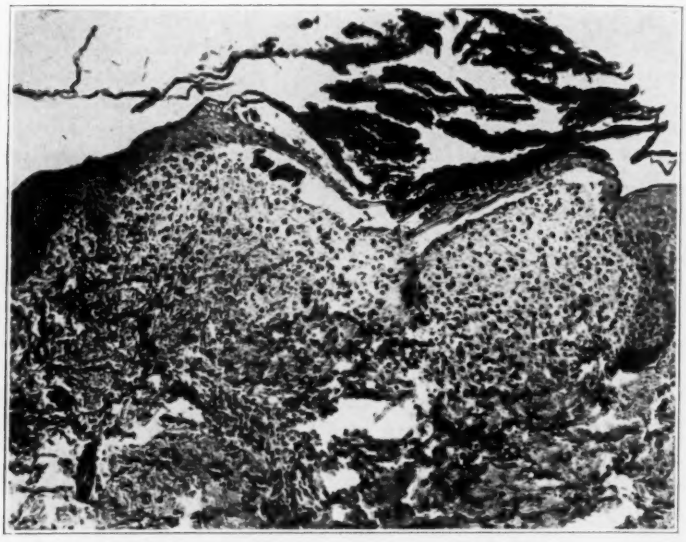

Fig. 4 (case 5).—Low magnification of a section from a pustular lesion.

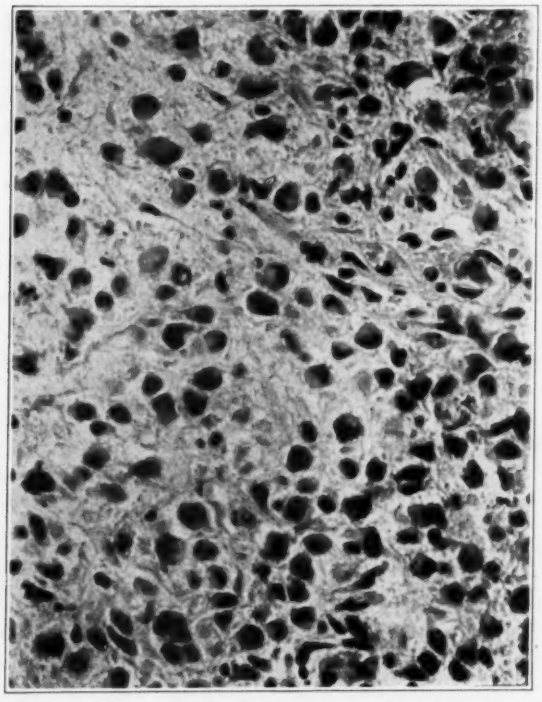

Fig. 5 (case 5).—Higher magnification of a section showing a loose structure with large reticular cells and many monocytes.

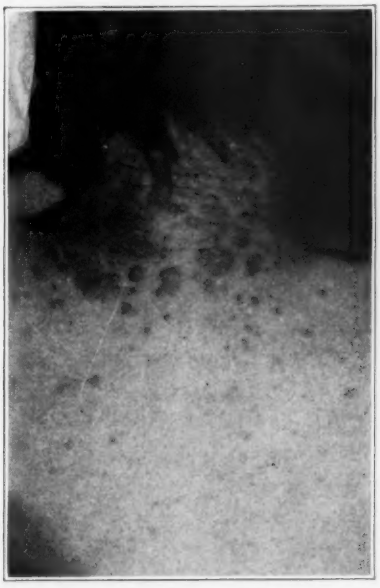

Fig. 6 (case 6).—The specific indurated papular eruption on the neck was accompanied by nodules on the arms and legs.

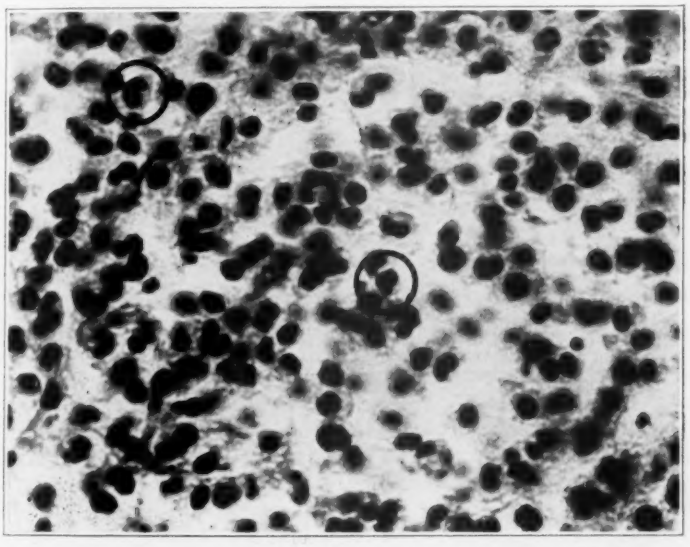

Fig. 7 (case 6).—The papules shown in figure 6 exhibit a close resemblance to the histologic changes seen in monocytic leukemia cutis and in acute reticuloendotheliosis. Note the adult monocytes as well as many immature cells and the loose reticular structure.

more such nuclei. In the middle third of the cutis there were some areas of necrosis and a heavy cellular infiltrate consisting of polymorphonuclear cells and small lymphocytes; larger cells having large, pale nuclei were attached to the reticulum (fig. 7).

Such papular and nodular eruptions are not infrequently observed in chronic reticulo-endotheliosis, but they do not have any specific clinical features. The earliest lesions on the neck resembled those of erythema multiforme because of the central edematous elevation and the surrounding papule.

Two other cases of reticulo-endotheliosis were observed in which the eruption was the most striking feature of the disease. The ulcerated lesions in these two cases were similar in appearance although the course was much less chronic in the first (case 7) than in the second (case 8).

Fig. 8 (case 8).—Chronic ulcers of reticulo-endotheliosis.

In the latter case the eruption was for many months the only demonstrable sign of disease.

CASE 7.—For six months a 28 year old man had been suffering from vague symptoms, such as transitory facial paralysis, swelling of the forehead which later subsided and weakness sufficient to interfere with walking. About one month before admission to the hospital there appeared on the face, neck and scrotum inflammatory lesions which broke down and discharged pus; he also suffered from fever and loss of appetite and of weight. There were generalized lymphadenopathy and splenomegaly. The skin was icteric, and there were numerous petechiae on the trunk and extremities. There was an eruption of the neck and cheek consisting of crusted ecthymatiform lesions. On the scrotum and thighs were ten punched-out necrotic ulcers having a profuse purulent drainage; not much inflammatory reaction was visible or palpable. The course was febrile. The blood counts on admission were normal though it was noted that the lymphocytes resembled those seen in benign lymphadenosis. Several days later the total number of white cells was 4,000, and 65 per cent were large, atypical mononuclears.

In addition to numerous lymphocytes and red blood cells, sections of skin showed many large mononuclear cells with dark reniform and bilobed nuclei. These cells were superimposed on a loose reticular structure.

CASE 8.—An 18 year old boy presented an eruption which began as a blister on the right calf and then darkened and enlarged to a lesion 3 cm. in diameter (fig. 8). During the following week the lesion dried and central sloughing occurred. A number of similar lesions appeared, and all stages of the eruption were visible on the left foot, face, neck and hands. The ulcerated lesions were sharply marginated and had a firm base with central necrosis; each lesion had a red areola. General examination demonstrated nothing of significance except a palpable spleen and enlarged axillary lymph nodes. The white blood cell count was 8,000, and the differential count showed 60 per cent lymphocytes. A culture of the blood was sterile. After a few days in the hospital the patient remained free from new lesions for two months; then lesions again appeared on the legs, the eruption being accompanied by a high fever. Repeated examination failed to establish a diagnosis. Cultures of the blood were repeatedly sterile.

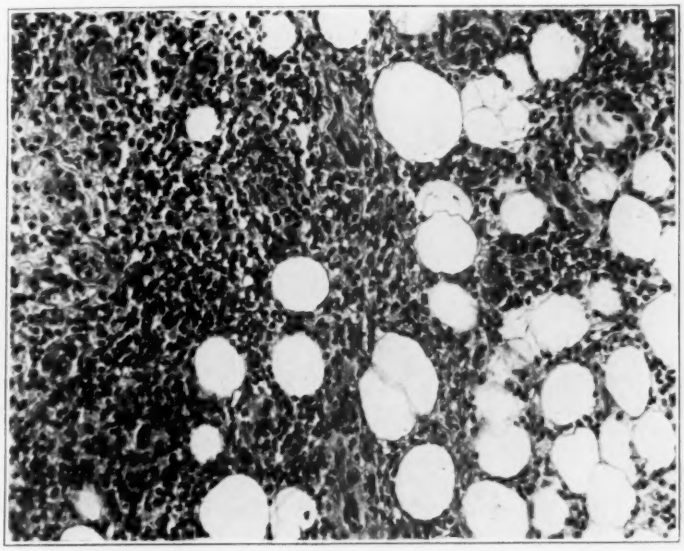

Fig. 9 (case 8).—Section from an ulcer of chronic reticulo-endotheliosis showing the resemblance to erythema induratum. Giant cells were present. The infiltrate consists of lymphocytes and granulocytes. The large clear cells in the upper right corner are reticular cells.

The fever was of a remittent character like that seen in cases of lymphogranulomatosis or typhoid. The Widal reaction was negative on several occasions. One month before he died the patient began to bleed from the nose and mouth, and at times he was irrational. He had several attacks of abdominal pain associated with distention. The white blood cell count ranged from 3,000 to 8,000, and the percentage of lymphocytes alternated between 30 and 60; there was no sign of immaturity of any of the white cells.

The cutaneous eruption became rather quiescent during the last weeks of life except that two lesions on the leg persisted as deep necrotic ulcers with overhanging borders; the largest was 7 cm. in diameter. A study of the lymph nodes at autopsy showed a diffuse reticular hyperplasia with some rounding out of the

reticulum cells suggesting that they might be taking part in blood formation. The bone marrow also showed numerous reticular cells. The final diagnosis was aleukemic reticulo-endotheliosis.

Tissue examined early in the course of the disease showed necrosis extending nearly to the subcutis. There was perivascular lymphocytic and polymorphonuclear infiltration at the borders, and the infiltrate was replacing the adipose tissue below. Nests of larger cells with clear, oval nuclei were at first regarded as epithelioid cells. There were also areas of hemorrhage (fig. 9).

Later in the course of the disease a new lesion showed almost complete replacement of the cutis by a loose reticulated granulation tissue with giant cells and an occasional large fat cell. There were areas of hemorrhage and some nests of lymphocytic infiltrate. Polymorphonuclear cells were also present. Within the loose connective tissue framework were many larger cells, some round

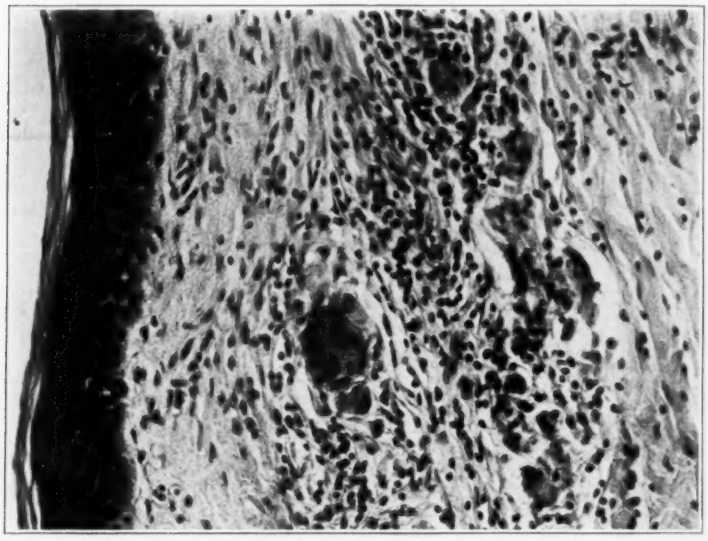

Fig. 10 (case 8).—Section removed later in the course of the disease, showing more specific changes with monocytoid infiltration.

and some irregular with projecting fibrillary processes. The multinucleated giant cells were fixed to the reticular framework by fibrillary processes. In a few areas the granulation tissue was more cellular and resembled a rather loose fibroblastic proliferation (fig. 10).

In the last two cases the disorder represents a necrotic ulcerative tendency which seems to have a few definite characteristics: There may be a history of preceding lesions, as in the case in which hemorrhagic bullae were observed (case 8) or the ulceration may be the first change noted. These ulcers are tender but not extremely painful. The base is flat and necrotic, the borders sharp and the edges undermined. The purulent discharge subsides in a few days, but the lesions persist

unchanged for many weeks. There is little surrounding inflammation. In the earlier months of the disease the lesions may heal with scarring. Later lesions persist and show no evidence of any tendency toward granulation or epithelization. In early stages the microscopic changes are inflammatory and associated with perivascular cellular infiltration, the presence of giant cells and necrosis. Later the tissue seems to lose its original power to react, and only a loose fibrillary granulation tissue is observed.

DIFFERENTIAL DIAGNOSIS

The diagnosis of monocytic leukemia presents no great difficulties. The angina, febrile course and hemorrhagic tendency make one immediately suspicious of acute leukemia, and the hematologic examination should establish the diagnosis. The cutaneous lesions are usually nonspecific, consisting of petechiae and areas of hemorrhage, although specific exanthems also occur. These macular and papular exanthems must be differentiated clinically from the syphilitic roseola and the macular exanthematous eruptions associated with acute and chronic infectious diseases. In the chronic forms of monocytic leukemia the subcutaneous nodules and the hemorrhagic tendency immediately suggest the necessity for study of the blood.

In cases of the strictly aleukemic forms of reticulo-endotheliosis antemortem diagnosis has seldom been possible, but a competent hematologist can recognize the liberation of reticulo-endothelial cells into the blood stream in some cases when the normal white blood cell count has not been exceeded. The necrotic ulceration observed in cases 7 and 8 seems to provide the most distinctive cutaneous feature in the chronic aleukemic phase. Microscopic examination of a cutaneous lesion may rule out other diagnostic possibilities, but the polymorphous cellular infiltrate, loose reticular structure and proliferation of the large cells of the reticulum have not previously been regarded as diagnostic.

Generalized papulonecrotic hemorrhagic eruptions provide the most striking clinical feature of acute aleukemic reticulo-endotheliosis. Such eruptions are not diagnostic, and one must consider a pyoderma associated with septicemia. In some instances, as in case 9, the diagnosis may not be clear until the internal organs have been examined.

Case 9.—A generalized eruption of six weeks' duration was observed in a child 5 months of age. The eruption consisted of small punched-out necrotic ulcers, from 0.5 to 1.0 cm. in diameter, some of which were hemorrhagic and some gangrenous. There were a number of infiltrated erythematous nodules on the forehead and eyelids. A few necrotic ulcers were seen on the palate. The white blood cell count was 1,700 and 2,500, respectively, on two examinations. Staphylococci were present in the blood and spinal fluid and in material from a furuncle; the internal organs showed evidence of staphylococcic septicemia.

In the upper portion of the cutis were many dilated vessels and a swollen cellular connective tissue. There was cellular infiltration with small and large mononuclear cells. Between the cutis and the subcutis were necrotic areas surrounded by an unusual granulation tissue having a loose edematous framework with polymorphic and lymphocytic infiltration as well as many larger cells with clear light-staining cytoplasm and round or oval nuclei.

This child presented necrotic lesions of the oral mucosa and a generalized eruption consisting of discrete papular and pustular lesions, many of which were hemorrhagic. The decreased white blood cell count was considered an aleukemic manifestation. A final diagnosis of staphylococcic septicemia was made after bacteriologic studies and sections of tissues had ruled out leukemia and reticulo-endotheliosis.

In case 10 there was a similar clinical picture consisting of a generalized pustular eruption, hemorrhagic tendency, septic course and a terminal decrease in the white blood cell count. There might have been considerable difficulty in classifying this eruption if the diagnosis of chronic myelogenous leukemia had not previously been established beyond doubt.

Case 10.—A boy aged 9 years had received treatment for chronic myelogenous leukemia for fifteen months when there developed an extensive furunculosis associated with an abscess of the axilla and septicemia. Culture of the blood and local lesions showed staphylococci. Hemorrhage into the furuncles resulted in heavy black crusting; there was also bleeding from the mouth and nose. The white blood cell count, which had been as high as 340,000, dropped to 300 during the last few days of life, and in the last twenty-four hours of the patient's life no white cells were seen in smears of the blood.

In the upper portion of the cutis there was considerable lymphocytic infiltration, and many red blood cells were seen; the elastic tissue was not disturbed. In the lower portion of the cutis and in the subcutis were many necrotic areas surrounded by loose edematous connective tissue the cells of which contained large, pale nuclei. There was some replacement of the adipose tissue by lymphocytic infiltrate. The microscopic picture was not that usually seen in furunculosis, nor was it identical with the specific cutaneous changes described in cases of myelogenous leukemia.

An additional instance in which knowledge of the early course was of help was one of generalized herpes zoster (case 11) occurring in a patient with chronic lymphatic leukemia. If the patient had not been seen until after the eruption had become generalized it would have been difficult to differentiate this eruption from the conditions previously described.

Case 11.—A 48 year old man who had been treated for chronic lymphatic leukemia for three years had received high voltage roentgen therapy on numerous occasions. Solution of potassium arsenite U. S. P. was also administered. Six weeks later there developed typical herpes zoster of the lower left portion of the thoracic region which developed into a generalized vesicular eruption (fig. 11)

and progressed to ulceration and hemorrhage. There were numerous lesions on the visible mucous membranes. There was a definite increase in the proportion of immature white blood cells during the rapidly fatal course of the disease.

Gross and microscopic examination of the nervous system showed no hemorrhage into the root of the thoracic nerve corresponding to the area of zoster, although there was some lymphocytic infiltration in the meninges and diffuse glial proliferation was observed. Sections of the skin did not differ from those in other cases of severe herpes zoster except by the presence of a few immature cells in the infiltrate at the base of the vesicles.

Spiegler [10] in 1908 described a case of lymphatic leukemia in the course of which generalized herpes zoster developed. A total of nineteen cases of such a condition have now been recorded, in only one of which it was associated with myelogenous leukemia. Somewhat similar disorders have been described by Barney,[11] Brünauer,[12] and Philadelphy and Haslhofer.[13] The eruptions have tended to be more severe than the usual generalized herpes zoster, being hemorrhagic or gangrenous in most of the cases and resulting fatally in nearly half of them. In cases in which death did not occur the eruption was frequently associated with an exacerbation of the leukemia.

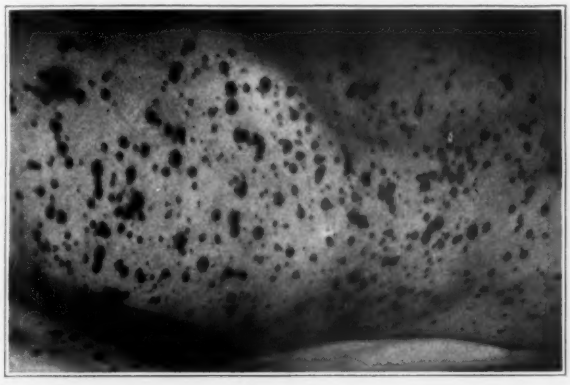

Fig. 11 (case 11).—Generalized herpes zoster in a patient with lymphatic leukemia. The vesicular lesions became hemorrhagic and necrotic, and the outcome was fatal.

Several attempts have been made to determine the cause of zoster eruptions in leukemia. Hemorrhage into the ganglion or lymphocytic

10. Spiegler: Wien. klin. Wchnschr. **21:** 156, 1908.

11. Barney, R. E.: Leukemia Cutis Resembling Herpes Zoster, Arch. Dermat. & Syph. **25:**1150, 1932.

12. Brünauer: Case Presentation, Zentralbl. f. Haut- u. Geschlechtskr. **46:** 413, 1933.

13. Philadelphy, A., and Haslhofer, L.: Varicellen bei leukämischer Lymphadenose, Arch. f. Dermat. u. Syph. **169:**502, 1934.

infiltration of the meninges or even of the nerve tissue has been observed. No changes which might be regarded as specific leukemic manifestations were found in the nervous system in case 11.

Damm [14] in 1931 and Katz [15] in 1932 reviewed the literature on zoster associated with leukemia; a total of twenty-seven cases are included in their reviews. Other cases have been reported by Craver and Haagensen,[16] Arzt,[17] Brandt [18] (two cases), Marcus [19] (two cases) and Proppe; [20] Zeisler [21] in 1928 mentioned having observed one case. In none of these cases was there any difficulty in recognizing the condition, but there is considerable similarity between the clinical appearance of these disorders and the generalized papulonecrotic eruptions associated with reticulo-endotheliosis. Case 11 of this series is reported not only because it is interesting in this respect but also because the disorder was an unusual leukemid which has not received the attention in the American literature which it appears to deserve. Montgomery [22] discussed it together with the nonspecific eruptions of the lymphoblastomas and was the first to mention it as a common observation.

PATHOLOGIC PROCESS

The pathologic changes observed in the specific cutaneous lesions of monocytic leukemia are rather characteristic. The epidermis is normal or nearly so; in the earlier lesions cellular infiltration is seen chiefly in the perivascular areas and surrounding the appendages. The character of this infiltration is the diagnostic feature, the reaction consisting chiefly of mature and immature monocytes (fig. 1). There are large cells having an abundant cytoplasm. The immature forms have dark nuclei, which may be reniform or bilobed; in the more mature cells there are large notched or oval nuclei and the cytoplasm is frequently

14. Damm, P.: Om den aetiologiske sammenhæng mellem zoster generalisatus leucaemi og varicellen, Ugesk. f. læger **93**:1279, 1931.

15. Katz, F.: Zoster bei Leukämie, Arch. f. Dermat. u. Syph. **164**:561, 1932.

16. Craver, L. F., and Haagensen, C. D.: A Note on the Occurrence of Herpes Zoster in Hodgkin's Disease, Lymphosarcoma and the Leukemias, Am. J. Cancer **16**:502, 1932.

17. Arzt: Herpes Zoster gangrenosus et generalisatus bei mit Arsen behandelter leukämischer Lymphomatose, Zentralbl. f. Haut- u. Geschlechtskr. **44**: 505, 1933.

18. Brandt: Herpes Zoster generalisatus, Acta dermat.-venereol. **14**:514, 1933.

19. Marcus, K.: Två fall av zoster generalisatus, ett vid lymfatisk leukemi och ett vid aleukemisk lymfadenose, Finska läk.-sällsk. handl. **75**:429, 1933.

20. Proppe, A.: Sammelreferate über Zoster, Dermat. Ztschr. **69**:39, 1934.

21. Zeisler, in discussion on Ormsby: Herpes Zoster Associated with a Generalized Varicella-Like Eruption, Arch. Dermat. & Syph. **17**:140 (Jan.) 1928.

22. Montgomery, H., in Christian, H. A., and Mackenzie, James: Oxford Medicine, New York, Oxford University Press, 1936, vol. 14, chap. 1-A, p. 336.

granular. Although the recognition of monocytes is essential for the diagnosis, even an inexperienced observer can recognize the polymorphous cellular infiltrate as being different from other pathologic processes. The notching of the nuclei and the large size of the cells distinguish the condition from lymphatic leukemia. The difficulty in differentiating monocytic leukemia from myelogenous leukemia is apparent from a study of the cases described in this paper; accurate cytologic knowledge is necessary, or one may depend on the hematologic diagnosis from smears of the blood (fig. 12). The absence of Dorothy Reed cells and eosinophils differentiates this disease from Hodgkin's lymphogranulomatosis.

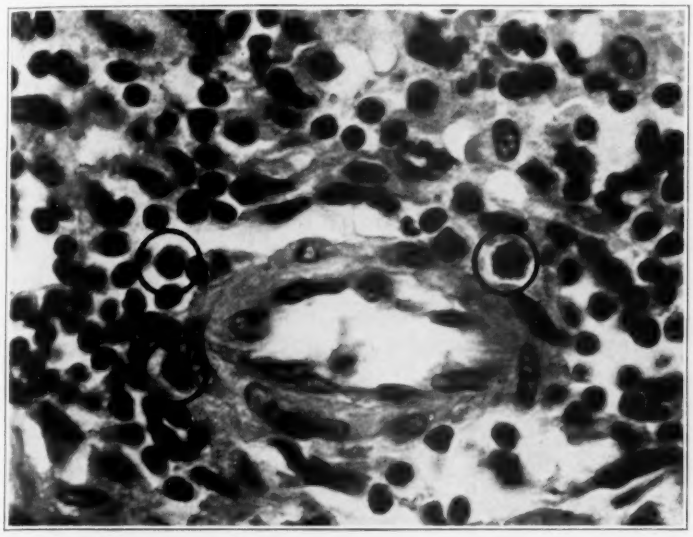

Fig. 12.—In myelogenous leukemia cutis the general structure resembles that of monocytic leukemia and reticulo-endotheliosis. The immature cells are difficult to differentiate, and large reticular cells are present in both conditions. The presence of immature and mature eosinophilic granulocytes as pointed out in a case of myelogenous leukemia seems to be the most obvious differential point.

Loveman [5] has pointed out that the cellular infiltrate extends between the connective tissue fibers and does not replace them as in the more solid areas of infiltration seen in other types of leukemia (fig. 2). He mentioned the irregular shape of the cells and the tendency to produce pseudopods, features which were particularly well demonstrated in the cases of chronic reticulo-endotheliosis described in this paper. He also emphasized the lack of practical value in application of the oxidase reaction to tissues removed from patients with monocytic leukemia.

There is fairly general agreement among the various observers as to the pathology of the cutaneous lesions of reticulo-endotheliosis. The

changes in the epidermis are secondary to disturbed nutrition. There is reticular proliferation in the cutis and infiltration with large mononuclear cells, observations which conform with the descriptions of the pathologic changes observed throughout the reticulo-endothelial system in cases of such disorders.

In sections from the skin of the patients whose cases are reported in this paper the early cutaneous changes appeared around the vessels and appendages of the skin and consisted of infiltration with small lymphocytes and polymorphonuclear leukocytes. At this stage the observations are not specific, although Bingel [23] mentioned that the general structure is looser than in lymphoma, this being apparently an early sign of the change in character of the connective tissue.

Later the involvement was most intense in the lower portion of the cutis and extended even into the subcutaneous tissue. The supportive tissues no longer resembled collagenous connective tissue; the fibrillary structure was replaced by a reticular network resembling embryonic mesenchymal tissue. Between the fibrils there were large round, oval or polygonal mononuclear cells some of which had long processes extending into the reticular network. The cytoplasm and nuclear structure stained lightly, and the nucleus was large and round or oval. In addition to these cells which seemed closely related to the reticular framework, there were round cells having a darkly staining small eccentric nucleus; such cells have also been described by Erber.[24] Many large clear cells having a moderately dense reniform or bilobed nucleus were observed; these cells resembled intermediate forms in the monocytic series (figs. 5 and 7).

Stains for elastin are of little help in the study of these diseases because they show only the absence of elastin fibers in the infiltrated and granulomatous areas and degeneration of these fibers in the corium at the border of the pathologic process.

In some instances of reticulo-endotheliosis large giant cells are observed, but they seem to be of no great aid diagnostically.

The pathologic changes observed in the skin of patients with reticulo-endotheliosis are easily distinguished from those of lymphatic leukemia.

The changes observed in the skin of patients with monocytic leukemia are similar to those of acute and chronic reticulo-endotheliosis. In certain phases of the lesions it seems impossible to differentiate these two diseases. In both there is a loose framework of reticular cells and fibrils, and the free cells are chiefly those of the monocytic series.

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23. Bingel: Monozytenleukämie? Deutsche med. Wchnschr. **42**:1503, 1916.

24. Erber, L. J.: Ueber sogenannte Retikulose mit Fettspeicherung, Virchows Arch. f. path. Anat. **282**:621, 1931.

In patients with myelogenous leukemia and also in infants suffering from acute sepsis similar processes may be observed. Under these conditions the connective tissues of the skin apparently return to their embryonal functional state and produce a reticular framework and immature free cells. The resemblance to reticulo-endotheliosis is even closer when a septic condition is superimposed on myelogenous leukemia (fig. 11). In none of these conditions is the proportion of monocytes in the infiltrate so high as in monocytic leukemia or reticulo-endotheliosis. In all of them the structure is less reticular and more cellular and mature fibroblasts are more numerous. The reason for the similarity of these pathologic changes is the close genetic relationship between reticulum cells, monocytes, histiocytes and fibroblasts.

The reticular proliferation and intermediate cell forms observed in the skin of patients with monocytic leukemia and reticulo-endotheliosis may be regarded as further support for the view that the specific cutaneous lesions of leukemia develop in situ and are not the result of metastases or infiltration from the blood stream.

HISTIOCYTOMA

Histiocytoma is described as a localized form of cutaneous reticulo-endotheliosis; the etiology and significance of this condition are not known. The histiocyte is regarded as a fixed connective tissue cell closely related to the monocyte of the blood because of their common origin from the reticulo-endothelial cell. The proliferating cells of histiocytoma are more highly differentiated than those observed in the cutaneous lesions associated with leukemic or aleukemic reticulo-endotheliosis, and the structure of the former is much more compact.

SUMMARY

No one theory of the differentiation of white blood cells is acceptable to all hematologists or pathologists. Downey's theory of such processes is particularly helpful in explaining the relationship between the monocytes and other cells of the blood and between monocytic leukemia and reticulo-endotheliosis. This theory is reviewed briefly, and the cases herein reported are discussed under his classification.

The clinical and microscopic observations in eight cases of monocytic leukemia and reticulo-endotheliosis associated with cutaneous changes are described.

The difficulties in the clinical diagnosis of generalized hemorrhagic papulonecrotic eruptions are emphasized by a comparison of such an eruption occurring as a manifestation of acute aleukemic reticulo-endotheliosis with furunculosis associated with myelogenous leukemia, with staphylococcic septicemia, and with a similar eruption which rep-

resented generalized herpes zoster in a patient with chronic lymphatic leukemia. Because of the interest in cases of zoster and leukemia reported in the foreign literature, the available information on this subject is summarized.

A type of chronic cutaneous ulceration observed in two cases of chronic reticulo-endotheliosis may be one of the characteristic lesions of this disease.

The essential feature of monocytic leukemia cutis is the infiltration with mature and immature monocytes. Such cells may be recognized by their large size and notched nuclei occurring together with other distinctive features. Acute or chronic reticulo-endotheliosis is characterized by the loose structure of the lesion; there are large reticular cells having vesicular nuclei, and within the reticular framework are large free mononuclear cells. A polymorphic infiltrate may be present.

The resemblance between the pathologic changes in the specific cutaneous lesions of monocytic leukemia and of reticulo-endotheliosis is regarded as further support for the view that reticulo-endotheliosis is an aleukemic manifestation of monocytic leukemia.

THE SUDORIPAROUS GLANDS

I. THE ECCRINE GLANDS

STUART C. WAY, M.D.
SAN FRANCISCO
AND
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Success in therapy for diseases of the skin demands a more intimate knowledge of the histology, physiology and function of the healthy skin. With this in view, the need for a careful study of the various dermal systems becomes apparent.

Mumford [1] emphasized the fact that constant changes are taking place in the superficial vascular system in response to various stimuli, and he expressed the belief that similar alterations are undoubtedly occurring in the activity of the sudoriparous glands, the output of which is subject to wide variations not only in different persons examined under similar circumstances but also in the same person examined at different times. These variations apparently depend on certain inherent physical and mental characteristics and on the metabolic requirements of the moment, resulting from altered internal or external physical influences or from both.

Steno [2] in 1683 seems to have been the first to mention the cutaneous openings of the sudoriparous glands; a year later Grew [3] also called attention to them. However, it was not until 1834 that the adult sweat glands were described by Breschet [4] and by Roussel de Vauzéme. Gurlt [5] in 1835 and Robin [6] in 1845 published valuable contributions on the subject.

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1. Mumford, P. B.: Simple Form of Sudorimeter, Brit. J. Dermat. **39**:256 (June) 1927.

2. Steno, quoted by Poirier, Paul, and Charpy, A.: Traité d'anatomie humaine, ed. 3, Paris, Masson & Cie, 1912, vol. 5, pt. 2.

3. Grew, quoted by Poirier, Paul, and Charpy, A.: Traité d'anatomie humaine, ed. 3, Paris, Masson & Cie, 1912, vol. 5, pt. 2.

4. Breschet, J., and Roussel de Vauzéme: Recherches anatomiques et physiologiques sur les appareils tégumentaires des animaux, Ann. d. sc. nat., September 1834, pp. 167 and 321.

5. Gurlt: Vergleichende Untersuchungen über die Haut des Menschen und der Haus-Säugethiere, besonders in Beziehung auf die Absonderungsorgane des Haut-Talges und des Schweisses, Arch. f. Anat., Physiol. u. wissensch. Med., 1835, p. 399.

(Footnotes continued on next page)

EMBRYOLOGY

The sudoriparous glands have a histogenesis similar to that of the sebaceous glands; thus two essentially different types are formed.

In the hairless regions the sudoriparous glands arise directly from the cutaneous ectoderm, while in the hairy regions the gland originates from the hair anlage. In the evolution of the rudiment of the sudoriparous gland in the hairless regions, three stages are recognized.

Stage of the Sudoriparous Rudiment.—In an embryo of the fourth month one notices first on the hands and feet full straight buds on the

Fig. 1.—A section from a 5½ month fetus, showing the ectodermal origin of a sudoriparous gland. To the right may be seen an early stage in sebaceous gland development. Hematoxylin and eosin; × 300.

top of the primary crests of the ectoderm, which are derived from the basilar layer. These buds are yellowish and grow perpendicularly into the dermis.

The absence of connective tissue around the epithelial bud suffices to differentiate the hair germ from the sudoriparous germ. The hair germ is further differentiated by its white color and its obliquity to the tegumentary surface.

6. Robin: Note sur une espèce particulière des glandes de la peau de l'homme, Ann. d. sc. nat., 1845.

The sudoriparous germinal layer appears first in the hairless regions and later in the hairy parts. Development occurs earlier on the palmar surfaces of the fingers than on the dorsal surfaces; this is especially true of the third finger.

During the fifth month the deeper extremity of the sudoriparous anlage becomes somewhat thicker, bending on itself to form a hook, the concavity of which is directed toward the surface of the skin. This hook twists on itself more and more.

Differentiation of the Excretory and the Secretory Segment.—The formation of the glomerulus begins at this stage. The secretory seg-

Fig. 2.—A section from a 6½ month fetus, showing a later stage in the development of a sudoriparous gland. The coil has partly formed. Note the sebaceous gland above. Hematoxylin and eosin; × 200.

ment, slightly thickened and solid at first, becomes hollowed out, forming a wide lumen which is limited by two rows of cells, one internal and one external. The first is made up of prismatically shaped glandular elements, while the second is made up of very thin cells, which later become myo-epithelial cells.

The lumen of the excretory duct appears during the sixth or seventh month, or after the formation of the lumen of the glomerulus. Some time elapses before the development of the vascular network which surrounds the gland.

Formation of the Excretory Orifice.—During this stage the gland becomes longer, and the glomerulus rolls up more and more. Up to this point the excretory segment, though hollowed out, does not open on the surface of the skin, nor is there any evidence at this time of a depression at its external termination. It is only in the seventh month (fetal) that there is a complete passage way through the epidermis. This passage way is in the form of a spiral, the turns of which become more and more numerous and the caliber of which becomes lessened. Sweat can appear on the surface of the skin as soon as the emissary orifices become opened. Because of the lateness of the time at which this occurs, one cannot believe that the sweat glands play a rôle in the formation of the amniotic fluid.

Sweat glands occurring in those regions covered with hair usually arise from the hair anlage. These glands appear at the same time as the hair germ and lengthen in the form of a cord much thinner than that of the hair. This cord appears above the rudiment of the sebaceous gland, later becoming hollowed out, and occasionally it pours out its secretion within the hair follicle. Usually, however, the gland gradually becomes separated from the hair follicle, its orifice moving away to open directly on the surface of the skin.

ANATOMIC, RACIAL AND OTHER CONSIDERATIONS

Morphology.—The sudoriparous glands are made up of a long tube, the deep end of which terminates in a cul-de-sac and the superficial extremity of which opens on the surface of the skin to form a pore.

The sudoriparous tube is made up of two parts: first, an excretory part, or glomerulus, which is rolled on itself like a ball, and second, a tubule made up of two segments and having the function of carrying to the outside products elaborated by the glomerulus. The deep segment pierces the corium in a straight or slightly curved line and is called the sudoriparous passage.

Location.—The sweat glands occur all over the surface of the skin, except on the anterior surface of the nails, the labia minora, the inferior parts of the labia majora, the internal surface of the prepuce, the glans and the internal part of the pinna of the ear. Some add to this list the skin of the eyebrow and parts of the integument where the muscles of the skin take their insertion, such as the region of the forehead, the cheek and the alae of the nose.

Everywhere else the sudoriparous glands are found at the surface of the skin, even on the caruncula lacrimalis and on the external surface of the pinna of the ear, where their presence was formerly denied.

Although the number of the sweat glands opening at the surface of the skin has been carefully estimated, there exists a wide variation in the count (from 2,000,000 to 15,000,000).

Their distribution is most uneven. They are rare on the external surface of the pinna of the ear and on the eyelids and are more numerous on the anterior than on the posterior surface of the body and the flexor than on the extensor surfaces of the limbs.

Sappey [7] counted 120 glands per square centimeter where the epidermis was thin, but this number increased to 371 where the epidermis was thick, such as the palms and soles. In the axilla they are supposed to be even more numerous.

Krause [8] counted the number of glands per square inch in various parts of the skin and found the following values: the soles, 2,700 per square inch (6.2 sq. cm.); the palms, 2,700 per square inch; the dorsum of the hand, 1,500 per square inch; the thorax, abdomen and arms, 1,100 per square inch; the dorsum of the foot, 900 per square inch; the cheeks and thighs, from 500 to 600 per square inch; the posterior surface of the neck, back and buttocks, from 400 to 600 per square inch.

Position and Size.—The glomerulus of the sweat gland can easily be recognized by its yellowish or pinkish color which makes it stand out from the white surrounding tissue. Its level in the skin is subject to considerable variation. Occasionally the glomeruli, alone or in groups of from four to six, occupy the entire thickness of the corium as on the nucha of the neck and the upper part of the back. In this location they are called intradermal. More frequently the glomeruli occur beneath the dermis within the panniculus adiposus, as on the extremities, hands, feet, areola of the mammary gland and genitals and in the axilla. In the palm the level of the glomeruli varies, and here they may be either intradermal or hypodermal.

The size of the sweat glands varies. They have been classed as large, medium and small, according to the volume of the glomerulus.

The larger glands are those occurring in the axilla and on the forehead. Their diameter varies from 1 to 4 mm. or more. The most voluminous glands are those on the nipple which hypertrophy during pregnancy. Medium-sized glands have a diameter from 300 to 500 microns and are found in the axilla and on the anterolateral parts of the body. Small glands are no larger than from 100 to 200 microns and are found on most of the parts of the body, either isolated or mixed with the large and medium-sized glands.

Racial factors are said to influence the size and number of the glands. In the Negro, whose skin resists high temperature, they are especially well developed, while the reverse is said to be true in the Fuegians.

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7. Sappey, M. P. C.: Traité d'anatomie descriptive, ed. 3, Paris, A. Delahaye, 1877, vol. 3, p. 594.

8. Krause, W.: Allgemeine und mikroscopische Anatomie, in Handbuch der menschlichen Anatomie, Hanover, Hahn, 1876, vol. 1.

Däubler [9] stated that the size of the sweat glands of the native of tropical Africa is much greater than that of the European. Anatomic differences, such as scanty body hair, highly developed and superficial blood vessels, everted lips and large nostrils, aid in combating the high temperatures of the tropics.

Aron [10] found that the sweating apparatus of the aborigines of the Philippines, the Negritos, is superior to that of the white race. This superiority is shown by the difference in the manner of sweating rather than in the amount of the sweat produced. The Negrito secretes small beads of sweat over the entire body, which soon form a thin film. As the whole surface of the body is covered by this watery film, the maximum cooling effect is obtained from evaporation.

In the case of the white man, on the other hand, sweating is practically limited to certain areas of the surface of the body. In these areas sweating may be quite profuse, but as most of the sweat drops off, comparatively little cooling results from the evaporation.

The most extreme individual variation is met in those cases in which the sweat glands are entirely lacking. Taendler [11] observed a man, aged 47, who had never perspired and whose body temperature rose as high as 40.8 C. (105.4 F.) when exposed to the sun's rays. In this case the whole ectoderm had suffered an arrest in development. The skin was smooth and thin and the teeth were limited to two incisors and two molars in the upper jaw, while the hair was extremely sparse. All the cutaneous glands seemed to be lacking, and even the hairs failed to have their accessory sebaceous glands. Injections of pilocarpine failed to cause any production of sweat.

HISTOLOGY OF THE ECCRINE GLANDS

The difference in the morphology of the glomerulus and the sudoriparous duct readily becomes apparent when one studies the histologic features of the two parts.

Glomerulus.—Under low power magnification, the glomerulus when sectioned appears to be formed of a number of cavities, placed side by side. These cavities, having a rounded or elliptic shape, are in reality only the cross-sections of the various segments of the glomerular tube.

Under a higher magnification one sees that the glomerulus is surrounded by a vitreous membrane, giving rise to two layers of cells, an internal and an external.

The basal layer of the sudoriparous glands is thicker (from 2 to 4 mm.) than the stratum lucidum of the epidermis, with which it is

9. Däubler, K.: Die Grundzüge der Tropenhygiene, Berlin, O. Enslin, 1900; cited by Aron.[10]

10. Aron, Hans: Philadelphia J. Sc. **6**:101, 1911.

11. Taend'er: München. med. Wchnschr., 1900, p. 1587.

continuous. It gives the same reactions as the latter, such as a blue color with hematoxylin. Its external surface is in relation with the connective tissue cells and the elastic fibers of the dermis. Its internal surface may occasionally have fine crests which interlock with those of the peripheral pole of the glomerular cells.

The external layer of the glomerular epithelium is made up of muscular cells of epithelial origin, that is, myo-epithelial cells. This is an unusual example of muscular tissue arising from the ectoderm. Placed between the basal layer and the internal cells of the glomerulus, these myo-epithelial cells appear fusiform, being directed obliquely to the axis of the tube, around which they describe an elongated spiral. Because of their obliquity, these muscular fibers act as longitudinal as well as circular fibers, thus having the power to shorten the secretory tube and at the same time to reduce its transverse diameter.

These myo-epithelial cells are composed of a cell body and a nucleus. The latter is elongated in the long axis of the cell, and, projecting on the internal surface of the cell, it comes in contact with the glandular cells. The cell body is composed of two parts: (1) a clear internal part surrounding the nucleus, called perinuclear protoplasm, and (2) an external fibrillary part, situated at one side and coming in contact with the basal layer. It represents a truly contractile element; its surface has long crests which encroach on the vitreous membrane and remain firmly attached to it.

Histologists are not in accord regarding the relationship between the myo-epithelial cells. According to Renaut,[12] they are placed as a continuous sheet and completely separate the glandular epithelium from the basal layer.

The glandular or internal layer of the glomerulus is made up of a single row of prismatic cells, placed perpendicular to the vitreous membrane. The base of these glandular cells is directed toward the periphery of the glomerular tube, where it comes in contact with the basal membrane when the myo-epithelial cells are absent at that point. When the muscular cell is developed, the glandular cells are either at a distance from the vitreous membrane or are attached to the vitreous by flat prolongations which wind in between the muscular cells so that they are surrounded by glandular elements on three sides. The apical pole of the sudoriparous cell is turned toward the lumen of the glomerulus, and its lateral surfaces are in contact with the lateral surfaces of the neighboring cells.

Fañanás [13] has shown by Golgi's method that the glandular lumen is prolonged between the two faces of adjoining epithelial cells, as inter-

12. Renaut, J.: Dispositif anatomique et mécanisme de l'excrétion des glandes sudoripares, Ann. de dermat. et syph. **5**:1101, 1894.

13. Fañanás, S.: Terminación de los tubos secretonos de las glándulas sudoriparas, Riv. trimest. microg. **1**:42, 1896.

cellular canaliculi, radial in direction, which can be followed to the neighborhood of the basal layer. The intercellular canaliculi, according to Poirier and Charpy,[14] are permanent structures surrounded by covering fillets. The intracellular canaliculi, however, are transitory structures excavated in the cytoplasm of the secreting cells.

The glandular cells have a rounded nucleus, with a nucleolus about half-way up the cell. A pair of micronuclei is located in the cytoplasm near the nucleus. The cellular body is bare; granules of various sizes are scattered in it, which are of two types, some being made up of fat while others, after being acted on by xylene and turpentine, are colored black with hematoxylin or osmic acid and are perhaps pigment granules.

Granules of unequal size, which stain red with carbolfuchsin, have been noted in the sudoriparous cells. As these granules reduce osmic acid after having been acted on by fat solvents, they cannot be regarded as fat granules, nor are they believed to be related to pigment.

However, a part of the cutaneous pigments reduces osmic acid as does fat. If treated first with chromic acid, this pigment, in contrast to fat, no longer reduces osmic acid.

Junction of the Glomerulus and Excretory Segment.—At the point where the excretory tube is a continuation of the glomerulus, the vitreous layer occurs without interruption. The myo-epithelial cells, which later disappear in the sudoriparous canal, are still present in this transitional zone and may have a bifurcated end. The epithelium proper presents here an unusual appearance with its two layers of cells. The cells of the deeper layer are polygonal or hemispheric and noticeable because of their large size and clearness. The cells of the superficial layer forming the edge of the lumen are small and deeply colored and usually have a thin extension which is insinuated between the deeply located cells and occasionally is prolonged to the myo-epithelial cells. The superficial part which surrounds the lumen appears as a refractile membrane.

Between the glomerulus and the excretory canal there is a zone of transition which is characterized by the fact that the glandular cells which are in one layer of the glomerulus have a tendency to become superimposed. Some of the cells become voluminous and keep their initial position, while others take on the shape of a nail, as though compressed by the deep cells. At the foot they are separated and intercalated between the deeper cells. Thus they are in contact with one another because of their flared-out head and constitute a continuous layer.

14. Poirier, Paul, and Charpy, A.: Traité d'anatomie humaine, ed. 3, Paris, Masson & Cie, 1912, vol 5, pt. 2.

The Sudoriparous Canal.—A slight thickening of the glomerular tube sometimes marks the beginning of the sudoriparous canal, which is formed of a double row of epithelial cells implanted on the basal layer. This basal layer of the canal touches on its external surface the connective tissue of the dermis and the elastic network which surround the sudoriparous gland. Two layers of epithelial cells are placed on the basal layer, the external one being continuous with the basal layer of the epidermis and the internal one lining the lumen of the canal.

The cells of the external layer are elongated and have a clear protoplasm similar to the cells of the external sheath of the hairs.

The cells of the internal layer are thicker; their free pole is surrounded by a narrow band and covered by a rigid membrane which is deeply stained by osmic acid. One concludes that there is no secretory phenomenon in the sudoriparous canal. Near the interpapillary epithelial bud the epithelium of the sudoriparous canal may be stratified and have from three to four layers. The canal itself is generally round or oval throughout its entire length.

The sudoriparous canal loses its wall as it enters the epidermis and is known as the sudoriparous passage. A simple opening, bordered on all sides by epidermal cells, makes up this sudoriparous passage.

In the malpighian layer this passage is either straight or rolled in the form of a spiral and limited by cells arranged in two or three concentric layers around the passage. These cells are flat and filled with granules of eleidin. The internal layer of these cells has a cuticle.

In the stratum corneum the sudoriparous passage forms a spiral with its turns close together and ends in a so-called sweat pore, which is placed obliquely to the surface of the skin.

In the dermis the course of the duct is more or less straight and almost vertical, that is, perpendicular to the surface of the skin. When the epidermis is thin, the duct runs through an interpapillary bud, traverses the malpighian layer in a straight line and spirals only within the stratum corneum to end in a pore.

When the epidermis is thick, as on the palms and soles, the dermis is furrowed with dermal crests the summit of which has two papillae. The sweat duct enters the epidermis at the summit of the epidermal bud, separating the two papillae. It twists on itself while penetrating the malpighian layer and describes from twenty to thirty circles of a spiral in the epidermis. These circles are constant and especially close together in the stratum corneum but are not exactly superimposed one on the other.

The cutaneous orifice of the excretory duct opens at the top of the papillary crests by a pore which has a double obliquity, that is, oblique to the surface of the skin and to the axis of the canal. Therefore, foreign bodies do not readily enter it.

Histophysiology of the Sweat Secretion.—Glandular and muscular cells form the essential parts of the glomerulus. These two types of cells may be activated separately through the influence of different agents, and it is possible to study the cellular modifications which accompany the secretory acts and the muscular contractions of the glomerulus. Heynold [15] has been given credit for the discovery that the glomerulus is responsible for the formation of sweat.

Secretory State: A gland which has just secreted an abundant amount of sweat has small and low glandular cells. The protoplasm is clear and shows no striations. The nucleus is large and forms the greater part of the cell. The lumen of the glomerulus is wide and filled with an irregularly shaped coagulum which is made up of slightly modified plasma. This plasma is of an albuminous nature and occasionally contains cellular débris. The periglandular connective tissue contains scattered red and white cells which may pass into the products of secretion.

Exhausted State: If the sudoriparous glands are examined while fixed in the contracted state, certain definite changes are noticed in the secretory part of the gland. This segment has a narrow, irregular lumen which is slightly smaller than normal. Certain modifications in the form of the glandular cells have taken place with reference to their structure and relation to each other. They are deformed and frequently flattened and contain large vacuoles. The cells on opposite sides of the gland come in contact with one another, so that the lumen of the glomerulus seems partitioned off by epithelial bridges. The myo-epithelial cells are in contact with each other, and because of their contraction a shortening of the glomerular tube occurs, which causes a narrowing of the lumen.

Periglandular Connective Tissue.—The connective tissue surrounding the gland is rich in elastic fibers. In the secretory segment one sees a few elastic fibers penetrating into the glomerulus, which are called intraglomerular fibers, but most of the fibers are placed around and perpendicular to the glomerulus so that a series of anastomosing rings are formed. These rings are attached to each other by longitudinal fibers, which limit their separation. In the dermal portion of the excretory canal the elastic fibers change their direction, so that they gradually blend with the elastic network of the papillary body.

Blood Vessels.—Many vascular twigs go to each glomerulus to form a network on its surface, the polygonal meshes of which measure from 20 to 40 microns. This network, because of its very richness, is distinguished from the vessels of the surrounding connective tissue.

Fine twigs from the periglandular network penetrate to the interior of the glomerulus, but they do not enclose the sudoriparous tube tightly in their meshes. All the glomerular vessels are embedded within con-

15. Heynold: Arch. f. path. Anat. u. Physiol. **61**:72, 1874.

nective tissue-forming arches, which are joined together by curved anastomoses.

The vessels of the excretory canal have two origins. Those destined to the deep part of the excretory canal come from the glomerular network, but those which supply the superficial part of the excretory canal come from the subpapillary plexus.

Lymphatics.—The lymphatics coming from the sudoriparous apparatus join the vessels from the subpapillary network.

Nerves.—Definite experimental proof of the existence of sweat nerves was first obtained by Goltz [16] in experiments on stimulation of the sciatic nerve in cats.

Early observers, including Herrmann,[17] Ficatier [18] and others, have shown that a rich nerve plexus exists around the gland which is made up of fibers without myelin; the fibers traverse the membrana propria and end in the musculature. The nerve fibrils have enlarged end-pieces, which come in contact with the excretory epithelium and are placed between the glomerulus and the excretory canal within the transitional epithelium.

Ranvier,[19] in speaking of the periglandular plexus, stated that this network is very fine and that its tight meshes are long and perpendicular to the long axis of the secretory tube. Some of the fibrils go forth from it to end in the myo-epithelial layer. Sfameni [20] in a later article stated that there is a nerve network in the membrana propria of the glomerulus which gives off fibers ending on the secretory epithelium. He expressed the belief that the nonmyelin network described by other writers is vasomotor in function.

Histologically and anatomically, the arrangement of the sweat fibers resembles that of the vasoconstrictor fibers, and, reasoning from analogy, one might suppose that a general sweat center exists, but positive evidence of such a center is lacking.

Howell,[21] in speaking of sweat centers in the central nervous system, stated that the fact that secretion of sweat may be brought about by stimulation of the afferent nerves or by direct action on the central nervous system, as in the case of dyspnea, implies the existence of

16. Goltz: Arch. f. d. ges. Physiol. **11**:71, 1875.

17. Herrmann, G.: Particularités relatives a la structure les glandes sudoripares, Compt. rend. Soc. de biol. **17**:365, 1879.

18. Ficatier, J. F. A.: Etude anatomique des glandes sudoripares, Thèse de Paris, no. 113, 1881.

19. Ranvier, L.: Le mécanisme des sécretions, J. de microg. **10**:544, 1886.

20. Sfameni, P.: Des terminaisons nerveuses dans les glomérules des glandes sudorifères de l'homme, Arch. ital. de biol. **29**:373, 1898.

21. Howell, W. H.: Textbook of Physiology, ed. 6, Philadelphia, W. B. Saunders Company, 1915, p. 861.

physiologic centers controlling the secretory fibers. The precise location of the sweat center or centers has not, however, been satisfactorily determined.

The action of the nerve fibers on the sweat glands cannot be explained as an indirect effect, for instance, as a result of a variation in the flow of blood. In human beings it is known that profuse sweating may often accompany a pallid skin, as in terror or nausea, while, on the other hand, the flushed skin associated with fever is characterized by the absence of perspiration.

There seems no doubt that the sweat nerves are genuine secretory fibers causing a secretion in consequence of a direct action on the cells of the sweat glands.

The sweat glands may be made to secrete in many ways other than by direct artificial excitation of the sweat fibers, for example, by extreme heat, dyspnea, muscular exercise and strong emotions and by the action of such drugs as pilocarpine, muscarine, strychnine, nicotine and physostigmine. In all such cases the effect is supposed to result from an action on the sweat fibers, either directly on their terminations or indirectly on their cells of origin in the central nervous system. If the nerves going to a limb are cut, exposure of that limb to a high temperature does not cause secretion, showing that the change in temperature alone is not sufficient to excite the gland or its terminal nerve fibers.

One must suppose, therefore, that high temperature acts on the sensory cutaneous nerves, possibly the heat fibers, and reflexly stimulates the sweat glands. Although external temperature does not directly excite the glands, it should be stated that it affects their irritability by direct action either on the gland cells or on their terminal nerve fibers.

Experimentation leads us to assume that there are spinal sweat centers, but whether these are few or represent simply the various nuclei of origin of the fibers to different regions is not definitely known. It seems reasonable to conclude that in addition to these spinal centers there is a general regulating center in the medulla.

HERPES ZOSTER GENERALISATUS

REPORT OF TWO CASES OCCURRING IN PATIENTS WITH LYMPHATIC LEUKEMIA AFTER TREATMENT WITH ROENTGEN RAYS

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Herpes zoster associated with a generalized eruption simulating varicella has been until recently a rather uncommon occurrence. In the greater number of cases reported the disorder has appeared in a patient with a disease belonging to the group of lymphoblastoma (Hodgkin's disease, lymphatic leukemia, myeloid leukemia, lymphogranuloma, etc.).

REPORT OF CASES

CASE 1.—M. H., a man aged 40, a furrier, born in Russia, came to the dispensary of the Jewish Hospital on April 19, 1933, complaining of swellings around the neck and in the armpits of three weeks' duration.

Family History.—The family history was irrelevant except for the fact that one brother had died of tuberculosis of the lungs at the age of 35.

Examination.—The glands of the neck were enlarged and swollen, the reaction extending to the angles of the jaw. Substernal dulness was noted. The spleen was enlarged from 2 to 3 fingerbreadths below the costal margin. The axillary and inguinal glands were also enlarged.

Examination of the blood gave the following results: The bleeding time was two minutes; the coagulation time, three minutes; the tourniquet test was positive. The hemoglobin content was 85 per cent. There were 70,000 platelets, 6,000,000 red cells and 36,000 white cells. The differential count showed 15 per cent polymorphonuclears, 0.8 per cent polymorphonuclear eosinophils, 1 per cent monocytes and 83 per cent small and large lymphocytes. The uric acid content of the blood was 3.5 Gm. per hundred cubic centimeters.

The basal metabolic rate (Sanborn) was + 57 per cent. The patient's height was 164 cm.; his weight was 87.5 Kg., and the surface area was 1.95 square meters. The duration of the test was fifteen minutes. The pulse rate was 76, and the respiratory rate, 17.

Roentgen examination of the chest showed considerable broadening of the superior mediastinal shadow, which had a nodular appearance. There was also

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Dr. Milton Wasch, director of the Department of Radiology of the Jewish Hospital, referred the patients.

From the Department of Dermatology and Syphilology of the Jewish Hospital, Dr. B. B. Berkowitz, Director.

a separate opaque mass extending from the root to the base of the right lung and adjacent to the cardiac border. No apparent involvement of the lungs was discernible.

Subsequent studies of the blood gave the following results:

	May 22, 1933	July 15, 1933	Sept. 1, 1933	March 23, 1934	Sept. 4, 1934
Hemoglobin	62 per cent	80 per cent	70 per cent	.....	59 per cent
Color index	.....	.....	.....	.....	0.8
Red cells	5,200,000	.....	4,600,000	.....	3,500,000
Platelets	70,000	.....	100,000	.....	.....
White cells	10,000	34,000	41,600	60,000	10,500
Polymorphonuclears	.....	15 per cent	17 per cent	15 per cent	12 per cent
Small and large lymphocytes	.....	85 per cent	83 per cent	85 per cent	88 per cent

Treatment and Course.—From June 28, 1933, to March 22, 1934, the patient received high voltage roentgen therapy to the enlarged glands and to the spleen. At that time examination showed enormous enlargement of all the lymph nodes—postauricular, cervical, mediastinal, axillary, inguinal and retroperitoneal. The spleen was enlarged, measuring 6 fingerbreadths.

The patient was seen again on April 2, 1934, at which time he presented an extensive eruption (see figure) beginning at the fifth lumbar and first sacral vertebrae on the left side and extending over the left hip and buttocks to the midline of the lower portion of the abdomen and the groin. The eruption consisted of groups of vesicles from 0.5 to 1 cm. in diameter, some of which had ruptured and many of which were gangrenous. The lesions were surrounded by a ring of erythema. Distributed over the entire body and over the face, trunk and limbs were numerous discrete vesicles, pustules and papules which simulated varicella. The mucous membranes were free from lesions.

The lesions of zoster cleared up, leaving pitted scars and pigmentations. The patient could not remember whether or not he had had varicella in childhood.

Case 2.—B. R., a woman aged 53, a housewife, was admitted to the Jewish Hospital on July 9, 1934, complaining of pain in the legs, generalized pain and weakness and difficulty in walking in a straight line.

Examination.—Examination showed enlargement of the inguinal and axillary glands on both sides. The liver and spleen were enlarged also. The Romberg sign was positive. When the patient walked she fell to the left.

The blood count showed 3,790,000 red cells, 64 per cent hemoglobin and 156,800 white cells. The differential count showed 1 per cent polymorphonuclears and 98 per cent small lymphocytes.

Repeated blood counts showed no change in the lymphatic condition.

Roentgen examination showed some turgescence of the anterior thoracic wall. Roentgen examination of the chest, however, showed no evidence of mediastinal tumor.

Neurologic study revealed a possibility of an intracranial lesion involving either the vestibular pathways or the cerebellum.

Treatment and Course.—The patient received high voltage roentgen therapy to the neck, axillae, inguinal regions, spleen and pituitary region for one year.

She returned to the hospital on July 20, 1935, after a rest of two weeks, complaining of burning pain and itching behind her right ear. She stated that she first noticed pimples on that area about one week previously.

Examination showed grouped vesicles, some of which were hemorrhagic and crusted, in the right postauricular region and extending on the posterior aspect

Varicelliform lesions distributed over the entire back. Gangrenous herpes zoster affecting the region of the fifth lumbar vertebra.

of the ear. Distributed over the left eyebrow, upper and lower lips, chin, chest, abdomen and back were numerous discrete papules and pustular lesions, some of which were surrounded by erythema. No lesions were found on the buccal mucous membranes.

COMMENT

According to Schoenfeld,[1] the first case of herpes zoster with aberrant vesicles was described by Lipp in 1889 at the congress of the German dermatologic society in Gratz, Austria. He described lesions of zoster affecting the trunk, arms and legs which appeared after a severe attack of zoster pectoralis.

Haslund [2] reported the case of a patient who presented herpes zoster affecting the left dorso-abdominal region and had vesicles on the trunk and extremities. This patient also had lesions on the tongue and mucous membranes.

Parounagian and Goodman [3] reviewed the literature to 1923 and reported only one case of herpes zoster with disseminated lesions occurring in a patient with lymphatic leukemia.

Fischl's [4] patient was examined post mortem, at which time there were found a generalized adenopathy and leukemic infiltration of the internal organs. The gasserian ganglions were found to be infiltrated with leukemic cells.

Jadassohn [5] presented a patient with herpes zoster and a varicelliform exanthem who had lymphatic leukemia. An attack of zoster gangraenosus in the region of the first and second branch of the trigeminal nerve was associated with a moderate varicelliform exanthema disseminated over the entire trunk. The patient stated that he had not had varicella. Jadassohn was of the opinion that the attack of herpes zoster had no connection with the lymphatic leukemia.

Jadassohn's patient was presented again three months later.[6] The leukemia had improved after roentgen therapy, but the patient had edematous swelling and redness on the face in the scars of the herpes zoster and more or less sharply limited, flat and elevated, irregularly round, bluish red and slightly transparent infiltrations. Surrounding the infiltrations were several lentil-sized red papules. Similar papules were disseminated on the trunk in the exact spots where vesicles had formerly been present. The lesions subsided somewhat after roentgen therapy, but they continued to be noticeable. Jadassohn could not decide whether the tumefactions were due to the blood residue or to the overgrowth of fixed elements in the skin.

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1. Schoenfeld, in Jadassohn, Joseph: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, p. 11.
2. Haslund, A.: Om zona, i anledning af et tilfälde med generaliseret eruption, Nord. med. Ark. **8**:1, 1897.
3. Parounagian, M. B., and Goodman, H.: Herpes Zoster Generalisatus, Arch. Dermat. & Syph. **7**:439 (April) 1923.
4. Fischl: Herpes zoster generalisatus, Wien. klin. Wchnschr. **24**:14, 1911.
5. Jadassohn, Joseph: Zentralbl. f. Haut- u. Geschlechtskr. **20**:23, 1926.
6. Jadassohn, Joseph: Zentralbl. f. Haut- u. Geschlechtskr. **20**:741, 1926.

Schreus [7] reported a case of herpes zoster occurring in a boy 11 years old after roentgen therapy had been administered for Hodgkin's granuloma. He believed his case to be the first instance of that condition reported.

Andrews [8] presented a man aged 29, who had been treated for Hodgkin's disease with roentgen rays and arsenic and had suffered from severe zoster of the left supra-orbital region.

Ginsburg [9] reported the case of a woman, aged 34, who after having received radium and roentgen treatment for Hodgkin's disease from July 1921 to January 1922 began to exhibit signs of spinal irritation. These signs became progressively worse until April 1923, when there developed a complete spastic paraplegia with sphincteral involvement. In July 1923 a profuse herpetic eruption developed. At first it appeared on the right side of the thorax at the level of the third and fifth dorsal segments of the spinal cord, and later it spread over the entire body, giving the appearance of typical chickenpox.

Pancoast and Pendergrass [10] described four cases of Hodgkin's disease in which herpes zoster occurred during the course of the malady. All the patients had received cross-fire roentgen radiation over the involved areas. The attacks of herpes zoster occurred from four months to five years after therapy had been instituted. In none of the cases were there any varicelliform lesions. Pancoast and Pendergrass stated that the occurrence of herpetiform eruption in patients with Hodgkin's disease was rare, but that such an eruption did occur more frequently than was generally recognized or taught.

Craver and Haagensen [11] recorded seven cases of herpes zoster observed among three hundred and twenty-nine cases of lymphosarcoma, Hodgkin's disease and leukemia and gave the figures as in the following tabulation:

Disease	Number of Cases	Number of Cases of Herpes Zoster	Percentage of Cases of Herpes Zoster
Lymphosarcoma	59	3	7.0
Hodgkin's disease	72	3	4.5
Lymphatic leukemia	108	1	0.9
Myeloid leukemia	90	0	0.0
Total	329	7	0.02

7. Schreus, H. T.: Dermat. Wchnschr. **83**:1606 (Oct. 30) 1926.

8. Andrews: Herpes Zoster Gangrenosa in a Patient with Hodgkin's Disease, Arch. Dermat. & Syph. **15**:736 (June) 1927.

9. Ginsburg, S.: Hodgkin's Disease with Predominant Localization in the Nervous System (Case 7), Arch. Int. Med. **39**:571 (April) 1927.

10. Pancoast, H. K., and Pendergrass, E. P.: On Occurrence of Herpes Zoster in Hodgkin's Disease, Am. J. M. Sc. **168**:326, 1924.

11. Craver, L. F., and Haagensen, C. D.: Occurrence of Herpes Zoster in Hodgkin's Disease, Lymphosarcoma and the Leukemias, Am. J. Cancer **16**:502 (May) 1932.

Craver and Haagensen did not describe a generalized varicella-like eruption in any of the cases they observed.

Halle [12] observed twenty-four cases of zoster in patients with leukemia. He noted that in the majority of cases herpes zoster appeared in male patients between the ages of 50 and 70 and that often it was accompanied by herpes generalisatus. The incidence is given in the following tabulation:

Type of Leukemia	Number of Cases	Male	Female	Number of Cases of Zoster Generalisatus
Lymphatic leukemia	16	13	3	11
Myeloid leukemia	5	5	0	1
Pseudoleukemia	3	2	1	0

Haack [13] reported a case of herpes generalisatus occurring in a 67 year old woman with lymphatic leukemia. She had had symptoms of lymphatic leukemia for one year when typical herpes zoster developed along the course of the fifth nerve. There was an associated generalized varicelliform eruption. Arsenic had not been given.

The diagnosis of herpes zoster generalisatus should be a comparatively simple procedure.

The primary lesions are typical and are usually limited to certain regions of the body. The groups of zoster lesions follow the course of the sensory nerves. Often the lesions are varied in appearance, and the eruption may be accompanied by fever, adenitis, pain and tenderness. New crops may appear after the outbreak of the primary lesions. Lesions may appear on the mucous membranes, but this is an uncommon occurrence. Nobl and Steuer [14] were the first to emphasize that varicelliform lesions may occur on the mucous membranes in association with an eruption of zoster. The generalized eruption simulates that observed in varicella.

PATHOGENESIS

It is generally believed that true zoster is always due to a specific virus. The disorder does not represent a trophic disturbance because the lesions develop in relation to the spinal ganglions. The eruption is probably due to the appearance of the virus at the level of the affected region. It appears that the skin is the portal of entry, whence the virus travels from the nerve endings, along the nerve sheaths, back to the spinal ganglions.

12. Halle, H.: Arch. f. Dermat. u. Syph. **159**:238, 1930.
13. Haack, K.: Dermat. Wchnschr. **95**:1819 (Dec. 17) 1932.
14. Nobl and Steuer, cited by Schoenfeld.[1]

According to Schoenfeld, there are three possibilities to be considered when herpes zoster is accompanied by a generalized zosteriform eruption:

1. The patient has a typical eruption of herpes zoster and gets an unrelated vesicular eruption.

2. The patient has a herpes zoster-like eruption which is only symptomatic of another condition already present which spreads as a vesicular eruption.

3. Primary herpes zoster becomes generalized owing to lack of resistance or lack of immunity of the host.

It has been shown that leukemic changes may occur in the spinal ganglion. This has been considered by many authors to be the chief rôle in the pathogenesis of zoster. Fischl [4] described a leukemic infiltration of the gasserian ganglion. Freund [15] described a case of zoster associated with hemorrhage about the gasserian ganglion and with degeneration in the ganglion. Marigonda [16] in examining spinal fluid observed an increase in the number of leukocytes similar to that in the blood and therefore concluded that the spinal ganglion was affected.

SUMMARY

Two cases of herpes zoster generalisatus occurring in patients with leukemia are reported.

Herpes zoster generalisatus followed high voltage roentgen therapy. One patient (case 1) had received roentgen radiation to the region of the spleen and involved lymph glands; the other (case 2) had received roentgen radiation to the cerebellar region because the possibility of leukemic infiltration causing symptoms was considered. It becomes more apparent that zoster with disseminated lesions is not infrequently observed in association with leukemia of the aged.

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15. Freund, H.: Arch. f. Dermat. u. Syph. **154**:476, 1928.
16. Marigonda, P.: Gazz. d. osp. **49**:549, 1928.

INFLUENCE OF SERUM ON THE FREI TEST

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As part of a study of lymphogranuloma venereum a series of experiments have been carried out to test the action of serum from patients with clinical manifestations at various stages of the disease on Frei antigen, when serum and antigen are administered intradermally to patients known to have the disease. These experiments were prompted in a measure by the report of Reiss [1] on the antigenic property of serum from patients with early stages of the disease and by the work of Gottlieb [2] on the neutralizing effect on Frei antigen of serum from patients with healing inguinal adenitis. While the work was in progress Haynes [3] reported the effect of serum from patients with lymphogranuloma venereum on Frei antigen, his report being based on results of intradermal injections of such serum in a small number of cases. He concluded:

> The mixture of Frei antigen and serum from a patient with lymphogranuloma inguinale produced the same cutaneous reaction as that to Frei antigen alone.
>
> The intradermal injection of serum from patients with lymphogranuloma inguinale into patients showing positive reaction to Frei antigen caused no reaction, with one doubtful exception.

It is well known that there is a great variation in the local and systemic response of patients to infection with lymphogranuloma venereum. While experimental work with mice and monkeys has shown that the virus is widely disseminated after inoculation and can be recovered

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1. Reiss, F.: A New Immunologic Reaction for the Diagnosis of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **31**:215 (Feb.) 1935.

2. Gottlieb, F.: Neutralisation du virus de la lymphogranulomatose inguinale (maladie de Nicolas et Favre) par le sérum des malades en voie de guérison. Méthode de contrôle de l'intradermo-réaction de Frei, Compt. rend. Soc. de biol. **111**:141, 1932.

3. Haynes, H. A., Jr.: Value of Intradermal Injection of Serum as a Diagnostic Test for Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **32**:795 (Nov.) 1935.

from the spleen, liver, kidneys and blood,[3a] there is no evidence to prove that this dissemination occurs in man, nor is there any conclusive proof that there is a natural immunity in man, partial or complete.

A positive Frei reaction means only that a patient has been infected with the virus of lymphogranuloma venereum and by the infection has been rendered allergic to the intradermal injection of the inactivated virus (Frei antigen). It appears that once the allergic state of the patient has been established it remains for life, though it is subject to some variation, as evidenced by the varying response of the same person to the same antigen at different times. Therefore, a positive Frei reaction demonstrates only that infection has occurred; it tells nothing about the activity of the disease in the patient tested.

The reports of Reiss, Gottlieb and Haynes raised many questions as to what, if any, demonstrable effect serum might have on the Frei test. Is the antigenic property of serum from a patient with an early stage of the disease more pronounced when the patient has an indolent, long-standing inguinal adenitis than when he has an acute infection? At what point in the healing of an inguinal adenitis do neutralizing bodies begin to appear in the serum? Does serum from a patient in whom no lesions have been present for more than a year still tend to inhibit the Frei reaction? Can serum from patients with late stages of the disease and with rectal strictures and esthiomene influence the Frei test? It was hoped that some estimation of the activity of the infection at a certain stage might be obtained by testing the effect of serum from a patient with that stage of the disease on Frei antigen when serum and antigen were injected intradermally into a patient in whom the duration and clinical activity of the disease were known.

There was another aspect of the problem on which it was hoped that some light might be shed. Repeated intradermal injections of Frei antigen have been recommended in the treatment of inguinal adenitis. If serum from patients receiving weekly injections of Frei antigen influenced the Frei reaction in other patients, some estimation of its value as a therapeutic measure might be forthcoming.

The same serums were being used to study the protection afforded by serum from patients known to have lymphogranuloma venereum when a mixture of serum and virus was inoculated into mice and guinea-pigs. As controls these mixtures of serum and virus were heated

3a. Findlay, G. M.: Climatic Bubo and Lymphogranuloma Inguinale, Lancet **2**:11, 1932; Experiments on the Transmission of the Virus of Climatic Bubo (Lymphogranuloma Inguinale) to Animals, Tr. Roy. Soc. Trop. Med. & Hyg. **27**:35, 1933. Levaditi, C.; Ravaut, P.; Lepine, P., and Schoen, R.: Récepticité de la souris à l'égard du virus de la maladie de Nicolas et Favre, Compt. rend. Soc. de biol. **109**:285, 1932. D'Aunoy, R.; von Haam, E., and Lichtenstein, L.: The Virus of Lymphogranuloma Inguinale, Am. J. Path. **11**: 737, 1935.

TABLE 1.—*Data on Serums Used for the Tests*

Patient	Race	Antigen Prepared From	Stage of Infection at the Time Blood Was Drawn or the Patient Was Used for Testing		Treatment	Date on Which Blood Was Drawn	Time After Appearance of Lesions	Experiment in Which Serum Was Used	Date on Which Serum Was Used	Number of Days Serum Was Stored at 4 C.
Br.	?	.....	Early	Inguinal adenitis	.....	6/25/35	2 weeks	1B	7/16/35 marked hemolysis	21
N. S.	White	.....	Early	Inguinal adenitis on right side healing; draining sinus still present 12/10/35	Intradermal injection of 0.7 cc. weekly of Frei antigen from 9/17/35 to 12/10/35; two courses of bismuth subsalicylate	9/ 5/35	3½ weeks	3A	9/24/35	19
								4	12/10/35	96
						9/17/35	5 weeks	3A	9/24/35	7
								4	12/10/35	84
						10/ 8/35	8 weeks	3B	10/ 8/35	0
								4	12/10/35	63
						10/15/35	9 weeks	4	12/10/35	56
						10/22/35	10 weeks	4	12/10/35	49
						10/29/35	11 weeks	4	12/10/35	33
						11/21/35	14½ weeks	4	12/10/35	19
M. G	White	8/29/35 glands	Early	Inguinal adenitis on left side; glands excised 8/27/35; wound healed 9/16/35	Intradermal injection of 0.7 cc. weekly of Frei antigen from 9/7/35 to 12/10/35	8/30/35	2 weeks	2, 3A	9/24/35	25
								4	12/10/35	102
						9/17/35	4½ weeks	2, 3A	9/24/35	7
								4	12/10/35	84
						10/ 8/35	7½ weeks	3B	10/ 8/35	0
								4	12/10/35	63
						10/15/35	8½ weeks	4	12/10/35	56
						10/22/35	9½ weeks	4	12/10/35	49
						10/29/35	10½ weeks	4	12/10/35	42
						11/ 7/35	12 weeks	4	12/10/35	33
						11/21/35	14 weeks	4	12/10/35	19
P. B.	White	.....	Early	Inguinal adenitis on right side; subsided without suppuration in two weeks	.....	11/ 5/35	1 week	4	12/10/35	35
A. Z.	White	.....	Early	Inguinal adenitis on right side healing; adenitis healed 6/4/35	Intradermal injection of 0.5 cc. of Frei antigen weekly from 4/13/35 to 6/4/35	5/16/35	6 weeks	1A	5/21/35	5
								1B	7/16/35	61
						9/17/35	22 weeks	4	12/10/35	84
						10/ 7/35	25 weeks	3B	10/ 8/35	1

A. A.	White	6/30/33 pus	Quiescent	Healed bilateral inguinal adenitis	Intradermal injection of Frei antigen, three doses of 0.3 cc. each, 7/13/25 and 9/6/35					
J. D.	White	.....	Quiescent	Healed inguinal adenitis on left side	Intradermal injection of Frei antigen, three doses of 0.3 cc. each, 3/28, 4/2 and 4/7/35	8/20/35	1 year 4 months	1C	8/20/35	0
M. S.	Negro	.....	Late quiescent	Rectal stricture	.....	3/15/35	Unknown number of years	1C	8/20/35	158
A. W.	Negro	.....	Late quiescent	Rectal stricture	Intradermal injection of Frei antigen, four doses of 0.4 cc. each, 3/7, 3/14, 4/25 and 5/2/35	3/15/35	6+ years	1C	8/20/35	158
F. S.	Negro	.....	Late quiescent	Rectal stricture; esthiomene	.....	8/20/35	10+ years	1C	8/20/35	0
H. J.	Negro	.....	Late	Perforations of labia and vagina	Bismuth and potassium iodide	5/16/35	Unknown 2+ years	1A 1B	5/21/35 7/16/35	5 61
B. S.	White	.....	Late	Rectal stricture; condylomas	Intradermal injection of 0.5 cc. of Frei antigen each week, Oct. 1934 to June 1935	5/16/35	Unknown 5+ years	1A 1B	5/21/35 7/16/35	5 61
J. Da.	White	.....	Late	Scar in left inguinal region; atrophy of left testicle, draining sinus in left portion of scrotum	Bismuth subsalicylate; intradermal injection of 0.6 cc. of Frei antigen each on 9/17 and 9/24/35	9/17/35 10/ 3/35	30 years	3A 4 3B 4	9/24/35 12/10/35 10/ 8/35 12/10/35	7 84 5 68
Normal controls: Repeatedly negative reactions to Frei antigen made from human pus										
H_1						8/20/35	.....	1C	8/20/35	0
H_2						9/24/35	.....	2, 3A	9/24/35	0
H_3						12/ 1/35	.....	4	12/10/35	9
S.						6/15/35	.....	1C	8/20/35	66

at 57 C. for the same time as in making Frei antigen and were injected intradermally into patients known to have lymphogranuloma venereum.

MATERIALS

Antigens.—Three antigens of different ages were used. The first, obtained from E. F. (case 2[4]), was prepared from pus aspirated on Oct. 17, 1934. The material for the second antigen was obtained at the first aspiration of pus from A. A. (case 4[4]) and had been stored in the icebox without appreciable loss of potency since July 1, 1933. The third antigen was made from an emulsion of a gland of M. G., Aug. 29, 1935.

Mouse Brain Virus.—Three mice of generation 11 of strain G died in convulsions twelve days after intracerebral inoculation. The brains were removed and a 10 per cent emulsion with Savita broth was prepared. This emulsion (163) was centrifugated for two minutes at low speed to remove the larger particles and the supernatant fluid was used for test purposes.

The brains of three other mice of generation 12 of strain G killed seven days after intracerebral inoculation were similarly prepared (emulsion 169).

The results of the inoculations of serum and virus into animals will be reported elsewhere.

Serums.—Details regarding the type and duration of the infection of the patients from whom the serums were derived, the amount of Frei antigen given intradermally, the antisyphilitic treatment given, the date on which the blood was drawn and the number of days which elapsed before the serums were used are given in table 1. Serum not used at once was stored in stoppered test tubes without a preservative at 4 C. and was always tested for sterility before being used. The normal serum was obtained from one of us (M. H.) on three occasions, the designations H_1, H_2 being used, and from a donor (S).

PROCEDURE

Equal parts of the antigen or of the emulsion of the virus used and of the serum to be tested were mixed, and 0.1 cc. was injected intradermally into patients known to have lymphogranuloma venereum. Control injections of undiluted Frei antigen, of equal parts of antigen and saline solution and of serum alone were employed. All the mixtures of serum and antigen were tested immediately after being prepared and, in most instances, after they had been allowed to stand for varying periods at 4 or at 37 C. In the case of the mixtures of serum and virus the material remaining after the inoculation of animals was heated in sealed tubes at 57 C. for two hours one day and for one hour the next day as is done in the preparation of Frei antigen. It was then kept in the icebox at 4 C. for ten days before the cutaneous tests were made.

All the cutaneous reactions were read and measured twenty-four and forty-eight hours after injection. An effort was made to use in any one experiment serum from patients with early and with late stages of the disease and to make tests on both patients with early and patients with late stages of the disease. Only the forty-eight hour readings are recorded in tables 2 to 5, which summarize the results obtained.

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4. Howard, M. E., and Strauss, M. J.: Lymphogranuloma Inguinale: Report of Sixteen Cases in and Around New Haven, New England J. Med. **212:** 323, 1935.

TABLE 2.—*Results of Tests*

Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum: A. Z.	B. S.	H. J.	Br.			Serum Alone: A. Z.	B. S.	H. J.	Br.
1A	5/21/35	E. F.	10/17/34	A. Z.	++++	++	++++	++++	++++	.....	.....	.....	0	0	0	..
				B. S.	++++	++	++++	++++	++++	.....	.....	.....	0	0	0	..
				A. W.	++++	++	++++	++++	++++	.....	.....	.....	0	0	0	..
1B	7/16/35	E. F.	10/17/34	A. A.	+++	++	++	++	++	++	.....	.....	0	0	0	0
				J. D.	+++	++	++	++	++	++	.....	.....	0	0	0	++(?)

Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum: Fresh Serum: Control H_1	J. D.	F. S.	Stored Serum: 66 Days Control S.	158 Days A. W.	158 Days M. S.
1C	8/20/35	E. F.	10/17/34	F. S.	+	++	+	++	+++	+++	+++	+++
				J. D.	++++	++	+++	++	+++	+++	+++	+++
							After Standing at 4 C. for 48 Hours					
	8/22/35		10/17/34	F. S.	+	+	+	++	+++	+	+++	+
				J. D.	++++	+++	+++	+++	+++	+++	+++	+++
							After Standing at 4 C. for 18 Days					
	9/ 7/35		10/17/35	M. G.	+++	++	+++	+++	N. D.	++	++	++

A reaction of from 2 to 3 mm. in diameter is indicated by +; one from 4 to 5 mm. in diameter, by ++; one from 6 to 7 mm. in diameter, by +++; 8 or more millimeters in diameter, by ++++.

RESULTS

In the first experiment (experiment 1A, table 2) serum from a patient with an early stage of the disease in the process of healing (A. Z.), which had been stored five days, and serum from two patients with late stages (B. S. and H. J.) were used; the cutaneous tests were made on the same patient with an early stage, (A. Z), and on two other patients with late stages (B. S. and A. W.). The serums alone failed to produce any reaction; the response to the mixtures of serum and antigen was greater than that to an equal dilution of saline solution and antigen used as control and was in each case equal to the results obtained with undiluted Frei antigen.

The same serums, stored sixty-one days, were again used (experiment 1B, table 2) to compare the results with those produced by serum from a patient with a very early stage of the disease (Br.).[5] The mixtures of serum and antigen were freshly prepared and injected within an hour into two other patients (A. A. and J. D.),

TABLE 3.—*Results of Tests*

Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum		
							M. G. 8/30	M. G. 9/17	Control H_2
2A	9/24/35	A. A.	6/30/33	M. G.	++++	++	++	++	++
				N. S.	++++	++	+++	+++	++
				J. Da.	++++	+++	+++	+++	++
	Incubated at 37 C. for 2 Hours; Kept in Icebox at 4 C. for 44 Hours								
2B	9/26/35	.....	.....	M. G.	N. D.	++	++	++	++
				N. S.	++++	++	++	++	++
				J. Da.	N. D.	++++	++	++	++

A reaction of from 2 to 3 mm. in diameter is indicated by +; one of from 4 to 5 mm. in diameter, by ++; one of from 6 to 7 mm. in diameter, by +++, and one of 8 or more millimeters in diameter, by ++++. N. D. indicates that the test was not done.

both of whom had healed lesions. The undiluted antigen produced a less marked response in these patients than in the previous three, but the mixtures of serum and antigen caused a reaction alike in all respects to that produced by the mixture of saline solution and antigen (control). It was not believed that the serum from the patient with the early stage of the disease (Br.) in any way enhanced the local action of the Frei antigen or that the serum itself possessed any antigenic properties. The serum was markedly hemolyzed on arrival, and an intradermal injection of it given to J. D., a patient with a healed lesions, resulted in a bluish red papule 4 mm. in diameter without surrounding erythema. This was fading at the end of forty-eight hours, at least four days before the reactions to the other tests made at the same time began to disappear.

The difference in the reaction produced by the mixtures of serum and antigen in experiments 1A and 1B raised the question whether the storing of serum for any length of time played any part in its action on the antigen. With this in mind experiment 1C was made. In this experiment the action of freshly drawn serum as compared to that of stored serum from normal persons as well as from patients with lymphogranuloma venereum was studied. Fresh serum was obtained from a normal person (H_2), from J. D., a patient with an inguinal adenitis which had been healed for over a year, and from F. S., a patient with a rectal stricture and elephantiasis of the external genitalia. Serum from a normal person (S) had been stored in the icebox for sixty-six days. Serums from A. W. and M. S.,

5. The serum was sent by Dr. H. M. Robinson, of Baltimore.

TABLE 4.—*Results of Tests*

Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum						Serum Alone					
							Control H_2	8/30 M. G.	9/17 M. G.	9/5 N. S.	9/17 N. S.	9/17 J. Da.	Control H_2	8/30 M. G.	9/17 M. G.	9/5 N. S.	9/17 N. S.	9/17 J. Da.
3A	9/24/35	M. G.	8/30/35	M. G.	+++	+++	+++	+++	+++	+++	+++	+++	0	0	0	0	0	0
				N. S.	+++	+++	+++	+++	+++	+++	+++	+++	0	0	0	0	0	0
				J. Da.	++++	+++	++	+++	+++	+++	+++	++	0	0	0	0	0	0
				Incubated at 37 C. for 2 Hours; Kept in Icebox at 4 C. for 44 Hours														
	9/26/35	.....	.....	M. G.	+++	++	+++	++	+++	++	+++	++	0	0	0	0	0	0
				N. S.	+++	++	+++	+++	+++	+++	+++	+++	0	0	0	0	0	0
				J. Da.	+++	+++	++	++	++	++	++	++	0	0	0	0	0	0
							10/8 M. G.	10/8 N. S.	10/7 A. Z.	10/3 J. Da.			10/8 M. G.	10/8 N. S.	10/7 A. Z.	10/3 J. Da.		
3B	10/ 8/35	M. G.	8/30/35	M. G.	+++	++	++	++	++	++			0	0	0	0		
				N. S.	+++	+	+++	++	+++	+++			0	0	0	0		
				Incubated at 37 C. for 3 Hours; Kept in Icebox at 4 C. for 42 Hours														
	10/10/35	.....	.....	M. G.	+++	++	++	++	++	++			0	0	0	0		
				N. S.	++++	++	+++	+++	+	+++			0	0	0	0		

A reaction of from 2 to 3 mm. in diameter is indicated by +; one of from 4 to 5 mm. in diameter, by ++; one of from 6 to 7 mm. in diameter, by +++, and one of 8 or more millimeters in diameter, by ++++.

both of whom had late stages of lymphogranuloma venereum with rectal strictures, had been stored one hundred and fifty-eight days. Tests were made with the freshly prepared mixtures after they had been left standing at 4 C. for forty-eight hours and for eighteen days, respectively. F. S. was a Negress with dark, thick skin, and the tests were made and the results read with difficulty, which may account in part for the variations in the cutaneous reactions recorded. From the results obtained it did not seem that serum from patients with lymphogranuloma venereum with clinically quiescent lesions had any greater effect on antigen when injected intradermally than did normal serum, regardless of the time it had been stored or of how long the mixtures of serum and antigen had stood (fig. 1). The irregularities present made it apparent that many more tests were necessary before a conclusion, if any was possible, could be reached.

TABLE 5.—*Results of Tests*

			Serum Used		Patients Tested					
					M. G.		N. S.		A. W.	
Date	Control	Mouse Brain Antigen	Case	Date Drawn						
12/10/35	Saline solution	169	.....	.....	+++		+++		N.D.	
	Saline solution	163	.....	.....		+		++		N.D.
	Normal serum	169	Control H_3	12/ 1/35	++		++++		N.D.	
	Normal serum	163	Control H_3	12/ 1/35		++		++		N.D.
		169	N. S.	9/ 5/35	+++		+++		+++	
		169	N. S.	9/17/35	++		+++		+++	
		169	N. S.	10/ 8/35	+++		++		++	
		169	N. S.	10/15/35	+++		+++		+	
		163	N. S.	10/22/35		+		0		0
		163	N. S.	10/29/35		+		0		+
		163	N. S.	11/21/35		++		+		+
		169	M. G.	8/30/35	++		+++		+	
		169	M. G.	9/17/35	+++		++		+	
		169	M. G.	10/ 8/35	+		++		+++	
		169	M. G.	10/15/35	++		+++		++	
		163	M. G.	10/22/35		+		+		0
		163	M. G.	10/29/35		++		+		0
		163	M. G.	11/ 7/35		++		++		++
		163	M. G.	11/21/35		+		+		++
		169	P. B.	11/ 5/35	++		+++		++	
		169	A. Z.	9/17/35	+++		+++		++	
		169	J. Da.	9/17/35	+		++		++	
		163	J. Da.	10/ 3/35		0		+		++

A reaction of from 2 to 3 mm. in diameter is indicated by +; one of from 4 to 5 mm. in diameter, by ++; one of from 6 to 7 mm. in diameter, by +++, and one of 8 or more millimeters in diameter, by ++++. N.D. indicates that the test was not done.

Experiments 2A and 2B (table 3) were made with an old but potent antigen and with serum from a control (H_2) and from a patient with an early stage of lymphogranuloma venereum obtained before the glands had been excised (M. G., Aug. 30) and two weeks later (Sept. 17) when healing of the operative wound was progressing satisfactorily. The tests were made on two patients with an early stage of the disease (M. G. and N. S.) and on one with an infection of thirty years' duration (J. Da.). Serum from a normal person and the antigen produced results similar to those obtained with the antigen and serum from a patient with an early stage of the disease, and neither mixture seemed to have an action greater than that which might be attributable to dilution (see control experiments with saline solution).

In experiment 3A (table 4) the tests were repeated with a freshly prepared antigen mixed with the same serums as those used in experiment 2 as well as

with serum from another patient with an early stage of the disease (N. S.),[6] from a patient with a late stage (J. Da.) and from a normal person (H_2). Tests were made with the freshly prepared mixtures and were repeated after the mixtures had stood for some time. It was not found that serum from the patients with early stages of the disease in any way enhanced the local action of Frei antigen or that the serum itself possessed any antigenic properties.

Fig. 1.—Frei reactions in J. D., experiment 1C (8/22/1935). The mixture of serum and antigen used had stood for forty-eight hours at 4 C. The results were: 1, reaction to undiluted antigen from E. F.; 2, reaction to antigen and saline solution; 3, reaction to antigen and fresh serum from a normal person; 4, reaction to antigen and fresh serum from J. D.; 5, reaction to antigen and fresh serum from F. S.; 6, reaction to antigen and serum from A. W. stored one hundred and fifty-eight days; 7, reaction to antigen and serum from M. S. stored one hundred and fifty-eight days; 8, reaction to antigen and serum from a normal person (S.) stored sixty-six days.

6. In this patient the glands were not removed surgically as in M. G. The bubo had been present for about two months, and suppuration was well advanced when he was first seen. On Sept. 4, 1935, 2 cc. of thick greenish yellow glairy pus was aspirated. A sinus developed at the site of the puncture and continued to drain until December 1935, though the bubo became progressively smaller.

Serum obtained at later dates from the same patients with early stages of the disease (N. S. and M. G.) as healing was advancing and from a patient whose lesion had been healed for some months (A. Z.), as well as serum from a patient with a late stage (J. Da.) when used in combination with Frei antigen (experiment 3B, table 4), produced reactions as irregular as those observed previously (fig. 2). No differences could be found in the effect of serum from the patients with healing lesions (M. G. and N. S.), with healed lesions (A. Z.) or with long standing lesions (J. Da.).

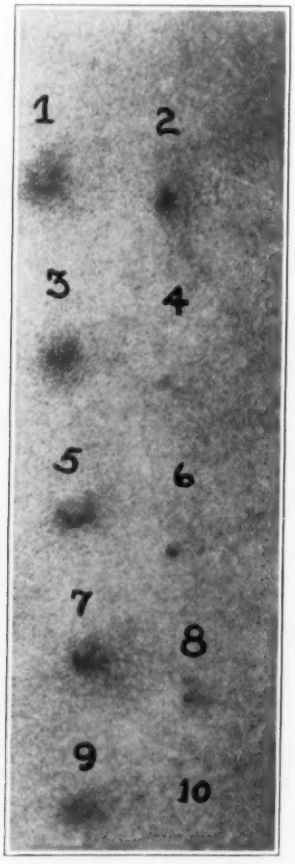

Fig. 2.—Frei reactions in N. S., experiment 3B (10/8/1935). Mixtures of serum and antigen were injected immediately after being prepared. The results were: 1, reaction to undiluted antigen from M. G.; 2, reaction to antigen and saline solution; 3, reaction to antigen and serum from J. Da. (10/3/35); 4, reaction to serum J. Da. (10/3/35); 5, reaction to antigen and serum from A. Z. (10/7/35); 6 reaction to serum from A. Z. (10/7/35); 7, reaction to antigen and serum from M. G. (10/8/35); 8, reaction to serum from M. G. (10/8/35); 9, reaction to antigen and serum from N. S. (10/8/35); 10, reaction to serum from N. S. (10/8/35).

Three of the patients had received intradermal injections of Frei antigen for about a month, two having received the antigen just prior to the time serum was drawn and the third having received it four months before. Two were receiv-

ing weekly intramuscular injections of bismuth subsalicylate. Therapy seemed to play no part in the results obtained.

The results of the mixtures of serum and virus made into antigens are shown in table 5. The antigenic properties of emulsion 163 (an emulsion of mouse brain) were considerably less than those of emulsion 169 but were consistently so in the control mixtures with saline solution, in the mixtures with normal serum and in those with the serums from patients with lymphogranuloma venereum tested. Serum had been collected from the two patients with early stages of the disease (N. S. and M. G.) at approximately weekly intervals for three months as healing progressed and while the patients were receiving weekly injections of Frei antigen intradermally. In N. S. the treatment did not seem to accelerate healing, as the sinus which formed about the site of puncture when pus had been aspirated from the gland continued to drain during this time. In M. G. the wound healed within two weeks after the glands had been removed, though this patient was also given continued weekly injections of Frei antigen. From the results obtained it did not seem that serum from patients with healing early lesions of lymphogranuloma venereum tended to suppress the action of Frei antigen. Nor was the difference between the reaction resulting from injection of serum from a patient with an early stage and an indolent lesion (N. S.) and the reaction following injection of serum from a patient with an early stage whose glands had been removed (M. G.) great or consistent enough to indicate that the variation was due to the clinical course of the disease. The continued use of Frei antigen in these patients did not seem to produce any effect that could be demonstrated when their serums were used in combination with Frei antigen in tests on other patients.

CONCLUSIONS

From a study of tables 2, 3, 4 and 5 it seems clear that serum from patients with lymphogranuloma venereum, regardless of the stage of the infection and of the amount or kind of treatment, had no greater effect on Frei antigen than had freshly drawn or stored normal serum. It was not found that serum from patients with early stages in any way enhanced the local action of Frei antigen nor that the serum itself possessed any antigenic properties. Serum from patients with healing lesions (A. Z., N. S. and M. G.) showed no greater inhibiting effect on the antigen employed than the factor of dilution might allow (see control experiments with saline solution), nor did the continued use of Frei antigen intradermally as a therapeutic measure seem to bring about any demonstrable change in the serum. The differences obtained seemed well within the limits of variation of any group of cutaneous tests.

SUMMARY

The effect of serums from normal persons and of serums from patients with various stages of lymphogranuloma venereum who had received various treatment on Frei antigen when given intradermally was studied. The tests were made on patients known to have lymphogranuloma venereum. No inhibiting or enhancing effects were observed.

DUST FROM DICTAPHONE CYLINDERS AS A CAUSE OF DERMATITIS

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During the past fifteen months we have had under observation a patient presenting a dermatitis caused by contact with the dust from dictaphone cylinders. Since, so far as we know, no description of this type of occupational dermatitis has been given, we are presenting a short résumé of this case.

Photograph showing marked edema of the face and of the eyelids following a severe flare-up of the eruption.

REPORT OF A CASE

W. T., a man aged 54, consulted us on Dec. 21, 1934, stating that intermittent attacks of dermatitis affecting his face, the backs of his hands and his ankles had occurred during the past eight years. The dermatitis sometimes developed suddenly and became severe enough to cause marked edema of the face and eyelids. At other times it receded and persisted for long periods as mild erythema and scaling. Periods of complete freedom had become less and less frequent in the last year or two. The clinical appearance of the eruption and the history of its behavior suggested dermatitis venenata. Questioning revealed that the disorder had first developed shortly after dictaphones were installed in the large business office in which the patient worked. Furthermore, his skin had cleared and remained well during a five month period several years before in which he had been away from the office and from dictaphones.

He was requested to bring some of the dust from his dictaphone as well as scrapings from the composition mouthpiece and from the cylinders for patch tests. He cleaned his machine and collected the materials the following day, and the next morning the dermatitis of his face flared up to the extent that his left eye was practically closed (fig.).

Patch tests applied to his arm revealed positive reactions to both the dust from his machine and the scrapings from the cylinders, the reactions to the latter being the stronger. Tests with scrapings from the mouthpiece gave negative results. Subsequently scrapings from two types of cylinders used revealed a 4 plus (vesicular) reaction to the scrapings of the cylinder labeled "master wax" and a slightly less marked reaction to the other. Tests with these substances gave negative results on controls. With the cooperation of Dr. N. K. Benton, medical director of the employees' benefit fund committee of the Western Union Telegraph Company, and of the Dictaphone Corporation, aluminum stearate, stearic acid and pine tar, three of the materials used in the manufacture of the cylinders, were obtained and used for patch tests. All gave negative results, however.

The patient was otherwise in good health. There was no personal or family history of allergy. His skin was clear save for a mild chronic interdigital fungous infection of the feet. Intradermal tests with trichophytin and oidiomycin (Lederle) in a 1:100 dilution provoked no reaction. Urinalysis gave negative results.

The patient was treated with soothing topical applications and fractional doses of roentgen rays. He carefully avoided all unnecessary contact with his dictaphone, which was kept carefully cleaned for him. He improved rapidly, and by Feb. 1, 1935, was well save for a slight residual thickening and scaling of his ankles and mild pruritus of his left eyelid. He remained well until May 11, when a severe flare-up occurred on his face and forehead. This was apparently the result of his being accidentally "showered" with dust from an adjacent machine. He then remained away from work until May 20, when the attack had partially subsided. On May 21, one of us visited him at his office. During the visit the mechanism of the machine and the arrangement of the "dust pan" were demonstrated in his presence. Apparently this was sufficient to cause another, though somewhat milder, flare-up. After this he remained away from work for several days. When he returned to work he was isolated from dictaphones entirely until the latter part of July 1935. Since then he has resumed work with a dictaphone but has been in a part of the office protected from drafts and isolated as completely as possible from his machine. All the machines in the office are carefully cleaned at night and are not disturbed during the day. Under this regimen the patient has remained free from dermatitis up to the present time.

A photograph showing a severe flare-up of the eruption is given.

LICHEN RUBER MONILIFORMIS (MORBUS MONILIFORMIS LICHENOIDES)

REPORT OF A CASE AND DESCRIPTION OF A HITHERTO UNRECORDED HISTOLOGIC STRUCTURE

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The prevailing general belief that so-called lichen ruber moniliformis is a variety of lichen planus does not receive support from our investigations of a dermatosis in many respects similar to the lichen ruber moniliformis originally described by Kaposi.

In the present report the name lichen ruber moniliformis is used mainly for the purpose of identification. Eleven biopsy specimens from our patient failed to reveal the usual histologic evidences of lichen planus.

An analysis of the cases recorded in the literature justifies the assumption that in nearly all those reported as instances of lichen ruber moniliformis the conditions were actually varieties of lichen planus. However, in a small minority the disorders certainly seem to belong in another category; of the latter group Kaposi's original case and our own case appear to be outstanding instances, since the conditions in these cases were not related to lichen planus or to any other conventional dermatosis.

Our interest in the case herein reported does not lie so much in the circumstance that it probably represents an instance of a hitherto undescribed dermatosis as in the fact that it confirms the contention of certain authors who asserted their belief in the nonrelationship of lichen ruber moniliformis to lichen planus.

KAPOSI'S ORIGINAL CASE

Kaposi [1] in 1886 described a unique eruption in a man, aged 45, who noticed the first signs of his cutaneous disorder fifteen years previously. The outstanding

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, Dr. George M. MacKee, Director.

Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936.

1. Kaposi, M.: Lichen Ruber Moniliformis, Vrtljschr. f. Dermat. **13**:571, 1886.

feature of the dermatosis was a striking and bizarre arrangement of waxy papules, nodules and keloid-like elongated strands forming parallel ridges chiefly on the neck and flexor surfaces of the arms and legs and disposed in conspicuous vertical rows corresponding to the long axes of the neck and extremities.

The similarity of the eruption to strings of pearls or of coral beads led Kaposi to apply the name lichen ruber moniliformis to this dermatosis. In addition to the elevated bandlike formations and contralateral depressions on the neck, arms and legs, there were many vertical linear lesions on the abdomen, back and buttocks and a retiform design of anastomosing, chainlike papular elements on the thighs. Other regions of the body, chiefly the chest, abdomen and back, were studded with innumerable small firm slightly elevated glistening brownish red papules, some of which had punctate central depressions. Pigmented spots having the appearance of sepia-brown puncta were profusely interspersed among the papular elements. There were no marks of scratching. Small flat papular lesions were discernible on the labial mucosa, while the buccal mucosa exhibited an adherent grayish yellow membrane. The genitalia were not affected.

In his description of the clinical manifestations Kaposi stressed the resemblance of many of the small elementary lesions to lichen planus. His study of the microscopic picture of lesions in different stages of development led him to conclude, on what is today regarded as flimsy evidence, that the histologic alterations pointed to an aberrant or anomalous variety of lichen planus. His accurate clinical and microscopic descriptions have a compelling merit; nevertheless, in the light of present knowledge a perusal of his article brings to mind the saying, "What we ardently wish, we soon believe." As a matter of fact, none of his sections exhibited the well recognized structural characteristics of lichen planus. The sections were studied by the elder Unna,[2] who wrote: ". . . neither the primary nor the secondary elements exhibit the structure of lichen planus. On the contrary, there is a complete disharmony between the clinical and the histologic diagnosis." Kaposi described a dense cellular infiltrate in the subpapillary portion of the corium without a trace of organization or connective tissue structure. Furthermore, fairly numerous giant cells formed a part of the infiltrate. The epidermis exhibited no pronnounced evidence of hypertrophy.

Unna's dissenting opinion has been upheld by subsequent authors. As early as 1905 Radcliffe-Crocker[3] said in his textbook:

. . . it is open to discussion as to whether these cases really belong to lichen planus; their general arrangement and the partial involvement of the face are against it, but Kaposi described it as a variety of lichen planus, and the others have followed him.

Kaposi's erroneous conception of the eruption he described is reflected in practically all the textbooks and in most of the contributions dealing with this and with seemingly related dermatoses.

2. Unna, P.: Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1924, p. 321.

3. Radcliffe-Crocker, H.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1905, vol. 1, p. 429.

In summing up the situation with respect to Kaposi's original case we are forced to conclude that the dermatosis was one which simulated some of the manifestations of lichen planus clinically but reproduced none of the characteristics of that disorder that are seen microscopically. This discrepancy impressed us strongly when we discovered that in our case, too, the eruption in certain respects simulated lichen planus clinically, but no evidence of that disease was disclosed on microscopic examination.

NOMENCLATURE

In the interest of brevity and to avoid irrelevancies a review of the literature [4] is omitted. Suffice it to say that a thorough search revealed sixteen articles and reports of cases with which the name lichen ruber moniliformis is linked.

Various designations have been utilized in connection with these moniliform dermatoses; among these are "lichen planus in anastomosing bandlets" (Dubreuilh); "lichen ruber moniliform lesions" (G. H. Fox); "lichen ruber acuminatus, verrucosus et reticularis" (Kaposi); "lichen universalis moniliformis" (von Düring), and several others.

The evidence strongly indicates that in nearly all the recorded cases the disorders were clinically aberrant or were anomalous manifestations of lichen planus, exhibiting diverse primary or elementary lesions which arranged themselves in more or less bizarre or eccentric patterns. These varieties have been familiarly designated as reticulate, anastomotic, zosteriform, striate, linear, banded and so forth. Most of them were rightly regarded as belonging to lichen planus associated with verrucous, hypertrophic, corneous, papillomatous, vegetating and other morphologically diverse elementary lesions.[5]

COMPILATION OF CASES

Of the sixteen cases reported in the literature the histologic observations are given in only seven; in these seven the microscopic examination revealed lichen planus of one or another variety with the exception of that present in Kaposi's original case. In the remaining nine cases microscopic reports are completely lacking, and the descriptions are for the most part so meager and sketchy as to permit only a nebulous visualization of the clinical features. Exceptions to the latter category are

4. For a review and summary up to 1923, see Sternberg, A.: Arch. f. Dermat. u. Syph. **143**:165, 1923. A complete bibliography up to 1921 is given by Bueler, F. A.: Arch. f. Dermat. u. Syph. **136**:117 (Sept. 12) 1921. There is an excellent discussion by Riecke, in Mraček, F.: Handbuch der Hautkrankheiten, Vienna, Alfred Hölder, 1905, vol. 2, p. 588.

5. In one case, Gunsett's, the retiform eruption of anastomosing bands corresponded in outline to the superficial veins of the lower portion of the abdominal wall and of the lower extremities.

the good clinical photographs of the disorder exhibited by two American patients, the case of one being reported by G. H. Fox [6] in 1888 and that of the other by Hyde [7] in 1906 and again by Hyde and Ormsby [8] in 1910. It is strange but true that these American patients exhibited eruptions more closely resembling those of Kaposi's and of our patient than did the disorders of any of the other patients, all of whom were Europeans. In view of the unquestionable clinical similarity of the eruptions to that in our case it is unfortunate that sections were not obtained in the two aforementioned instances. For purposes of comparison the clinical-morphologic features alone lend themselves to interpretation.

REPORT OF A CASE

Mr. C. H., a man aged 38, a native of the United States, a florist, first consulted Dr. William D. Whitehead, of Scranton, Pa., in March 1935 regarding his eruption. Dr. Whitehead removed several sections of the patient's skin for microscopic examination, sending the tissue to Dr. J. Frank Fraser, of New York, for study. (Dr. Fraser did not submit a report of his histologic observations.) The patient, having changed his residence to New York, applied for treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 29, 1935.

The patient's family history was irrelevant. Physical examination revealed an appendectomy scar resulting from an operation performed in 1921. The patient was operated on for hemorrhoids in 1924 and underwent a tonsillectomy in 1926. Since that date he had been in excellent general health except for his cutaneous disease. There was no history or evidence of venereal infection.

Examination.—Examination of the heart revealed bradycardia and left axis deviation. The basal metabolic rate was 7 per cent below normal. The blood pressure was 106 systolic and 80 diastolic. The patient's height was 72 inches (1.82 meters), and his weight, 162 pounds (73.5 Kg.). The pulse rate was 56 and the respiratory rate 16. Examination of the fundi showed that the nasal portions of the outline of the disks were blurred; otherwise the fundi were normal. The pupils were regular and reacted normally.

Roentgen examination of the skeleton revealed that the long bones were normal and the pelvis showed slight asymmetry. The sella turcica was proportionately large, being fully 20 per cent oversized in the ventrodorsal diameter; no evidence of erosions or pressure atrophy was discernible; small flecks of calcification in the pineal body were mesially placed and of no pathologic significance. Developmental variation was considered ascribable to slight glandular dysfunction; the hypophysis was relatively large. The sinuses and maxillary antrums were normal, except for slight clouding of the right maxillary antrum.

Cutaneous Condition.—The eruption was generalized, involving all regions with the exception of the anterolateral aspects of the cheeks, the nose, a portion of

6. Fox, G. H.: Lichen Ruber with Monileform Lesions, J. Cutan. Dis. **6**:312, 1888.

7. Hyde, J. N.: Lichen Ruber Monileformis, J. Cutan. Dis. **24**:85, 1906.

8. Hyde: Lichen Ruber Moniliformis, J. Cutan. Dis. **28**:265, 1910. Ormsby: Lichen Planus Atrophicus, ibid. **28**:467, 1910.

Fig. 1.—Lichen ruber moniliformis on the left arm.

Fig. 2.—Lichen ruber moniliformis on the right arm.

the subclavicular area and of the upper part of the sternal area of the chest, the interscapular portion of the back, the palms and soles and the glans penis. The visible mucosa and the nails were unaffected. The hair of the scalp was normal.

The areas exhibiting the most conspicuous features of the eruption were the forehead, the skin below and behind the ears, the neck, the flexor aspects of the upper extremities, the backs of the hands, the axillary regions, the abdomen, the thighs, the buttocks and the lower portion of the back. The lesions were more widely scattered and less prominent on the lower extremities, from the knees to the toes. The scalp exhibited a few scattered papules. Two postoperative scars on the abdomen were entirely free from papular lesions.

Fig. 3.—Lichen ruber moniliformis on the upper portion of the right arm.

The elementary lesions consisted of waxy papules varying from 1 to 3 mm. in diameter. Their outlines were round and dome shaped. The papules were of two types: (1) dark red and bright red elements and (2) waxy yellow milia-like elements. The red papules formed the greater part of the eruption, being present chiefly on the upper extremities, the abdomen, the back, the buttocks and the thighs. The waxy yellow papules affected chiefly the face, the periauricular areas, the middle portion of the chest and the scapular regions. All the red papules were larger, in the aggregate, than the waxy yellow papules; the latter did not exceed 2 mm. in diameter. The papules were smooth and devoid of surface markings such as scales, epidermal striae or dell formations. On the face, upper portion of the back and middle portion of the chest the smaller waxy yellow elements were intermingled with the red ones. On the other areas of the body

only the red lesions were apparent except on the shaft of the penis and on the scrotum; here the papules were lighter than the normal skin on which they were situated.

The consistency of all the papular elements (with the exception of those on the genitalia) was that of a keloid; the palpating finger received the impression felt

Fig. 4.—Lichen ruber moniliformis on the right hand.

when one presses a finger-tip on a solid rubber ball; the papules imparted a sensation of resiliency but did not feel "shotty." The lesions on the genitals, however, were soft to the touch.

On the chest, abdomen, buttocks and genitals the papules were relatively scattered, with normal skin intervening. In other regions, as on the glabella, below the lobes of the ears, on the flexor aspects of the upper extremities, on the backs of the hands and on the external aspects of the thighs, they were closely aggregated but not fused, thus forming a mosaic.

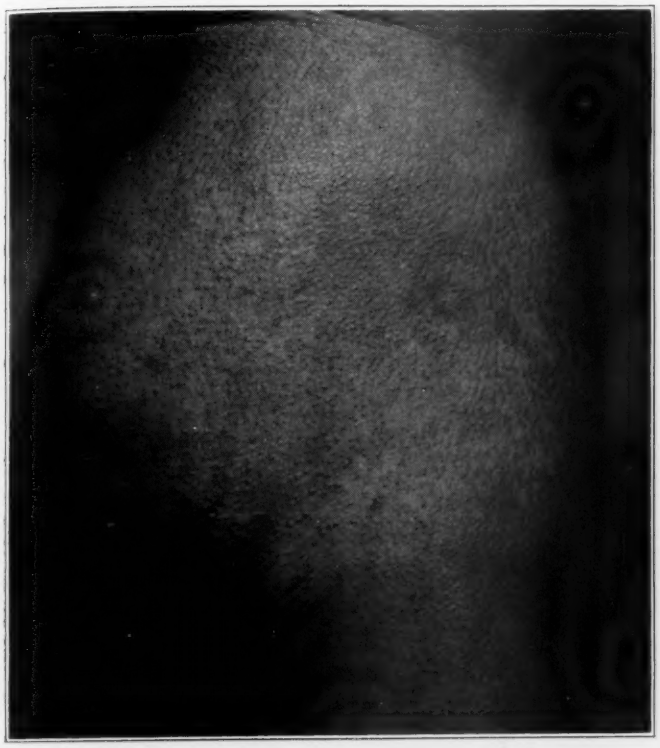

Fig. 5.—Lichen ruber moniliformis on the right buttock.

Fig. 6.—Lichen ruber moniliformis on the back of the neck.

The most prominent moniliform patterns were located on the antecubital areas, the back of the neck at its base, the anterior and posterior axillary folds and the anterolateral aspects of the upper part of the thighs. In the antecubital areas, extending half-way down the forearms and half-way up the arms, the papules gave the impression of having become fused to form fluted narrow keloid-like bands running parallel to the axis of the limb; these bands were most pronounced in the antecubital hollows, gradually shading off toward the less implicated skin on the wrist and middle portion of the arm. These longitudinal keloid-

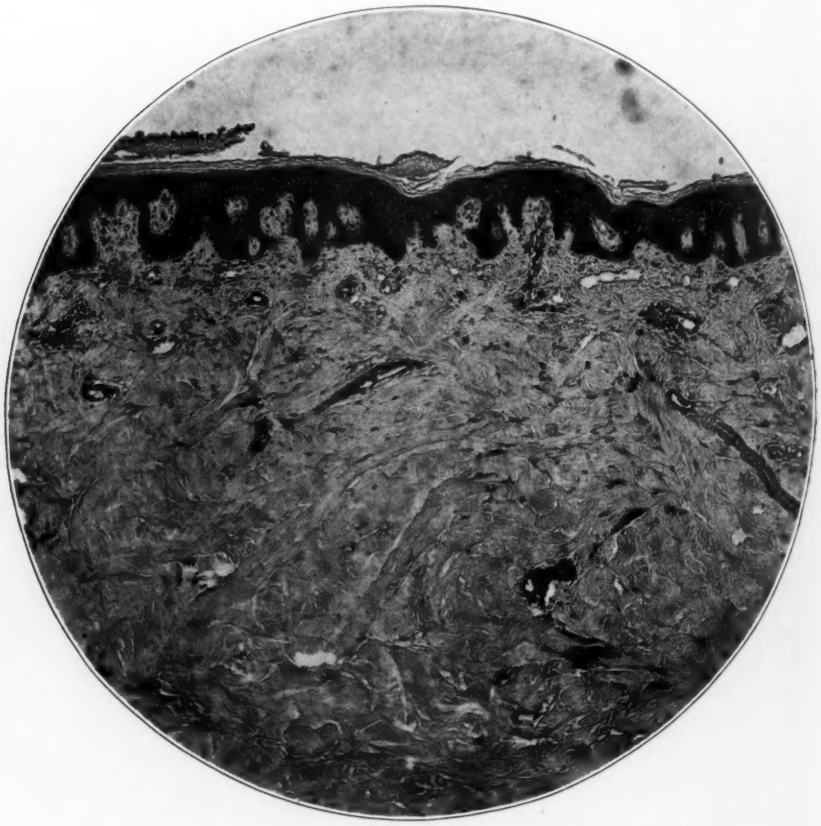

Fig. 7.—Low magnification of specimen examined on Oct. 2, 1935. The active process is predominantly in the upper portion of the cutis; the deeper layers of the cutis show a moderate degree of interstitial and parenchymatous edema.

like strands exhibited more or less well defined cross-hatchings, indicating the lines of contact between the adjacent papules of which the strands were composed. In these areas the red color was of a more dusky hue than elsewhere. In the other regions mentioned as sites of moniliform patterns the beaded arrangement was conspicuous but the keloid-like strands were absent and there was no indication of fusion of the elements or of cross-hatching.

Where the papules were closely aggregated and there were narrow zones of intervening normal skin the appearance of the eruption was suggestive of the surface markings of certain lizards.[9]

Subjective symptoms consisted of a moderate degree of itching, especially in warm weather. Marks of scratching were not observed at any time.

Treatment.—This was continued diligently over a period of three months and consisted of injections of arsenic in increasing doses, application of filtered and unfiltered roentgen radiation to various parts of the body and different topical

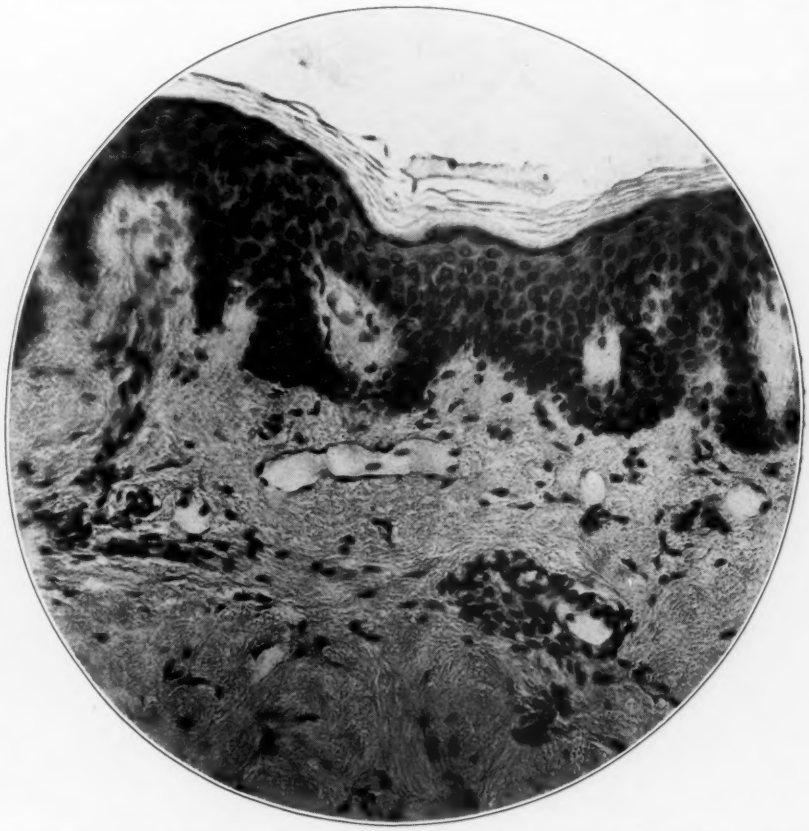

Fig. 8.—High magnification of part of the section shown in figure 7, showing dilatation of vessels and perivascular lymph spaces and of lymphatics in the upper portion of the cutis and occlusion of some of the vessels and degeneration of vascular walls.

applications. The result was disappointing; there was no visible alteration in any of the treated areas, although the patient fortunately had the impression that his eruption showed signs of improvement.

Laboratory Investigations.—The routine examinations of the blood and urine revealed no significant deviations from the normal. The Wassermann, Kahn,

9. It resembled particularly the appearance of the beaded lizard, known as the Gila monster.

Kline diagnostic and Kline exclusion tests were negative. The blood cell count showed 4,700,000 red cells, 5,200 white cells and 92 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclear leukocytes, 49 per cent; lymphocytes, 43 per cent; monocytes, 1 per cent; eosinophils, 5 per cent; myelocytes, 2 per cent. Chemical examination of the blood gave the following results: urea nitrogen, 9 mg.; sugar, 100 mg.; cholesterol, 185, and chlorides, 485 mg., per hundred cubic centimeters.

Estimations of the cholesterol content of the blood were made by Dr. Isadore Rosen.[10] The values obtained and the normal values are given in the following tabulation:

	Patient	Normal
Total lipids, mg. per 100 cc.	1,660.0	1,510 ± 91
Total cholesterol, mg. per 100 cc.	254.0	212 ± 18
Cholesterol esters, mg. per 100 cc.	140.0	152 ± 19
Free cholesterol, mg. per 100 cc.	114.0	59 ± 6
Free cholesterol (percentage of total cholesterol)	45.0	28 ± 4
Lipid phosphorus, mg. per 100 cc.	7.6	8.1 to 9.6
Albumin, Gm. per 100 cc.	3.9	4.8 ± 0.3
Globulin, Gm. per 100 cc.	2.5	2.6 ± 0.1

Dopa stains, investigations of amyloid and lipoid content of the skin, nerve fiber stain and studies for evidence of infection by bacteria and virus were made by Dr. Arthur W. Grace. To ascertain whether the infiltrate contained cells giving a positive reaction to dopa, frozen sections were stained with the dopa reagent by the method of Laidlaw and Blackberg.[11] No such cells were present in the infiltrate.

Sections covered with paraffin and fixed in solution of formaldehyde were stained by Roger's method for nerve fibers on the assumption that the lesion might represent an unusual type of nevus, as described by Masson.[12] No nerve fibers, however, could be demonstrated.

The superficial resemblance of the clinical manifestations to cutaneous amyloidosis prompted a search for amyloid and lipoid material in the lesions. Frozen sections were stained with sudan IV, and 0.1 cc. of a 1 per cent solution of congo red was injected into a group of lesions. No portion of the sections retained the sudan stain, and the congo red was not absorbed macroscopically by any of the lesions into which it had been injected; in fact, the lesion was apparently less stained by the congo dye than was the surrounding healthy skin. Sections stained with methyl violet did not reveal amyloid in any constituents of the tissue.

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10. The total lipid content was determined by extraction with alcohol and ether and by extraction with evaporation in a weighed casserole. The total cholesterol content was determined by a modification of the procedures of Myers and Wardell as described by Krasnow and Rosen (J. Lab. & Clin. Med. **14**:967, 1929); the ester and free cholesterol content, by a modification of the procedures of Bloor and Knudson as described by Rosen, Krasnow and Lyons (Cholesterol and Lecithin Studies in Syphilis: Cholesterol Partition in Relation to Wassermann Reaction, Arch. Dermat. & Syph. **27**:383 [March] 1933); the lecithin content, by the method of Krasnow, Rosen and Porosowska (J. Lab. & Clin. Med. **20**:1090, 1935), and the protein content, by the method of Greenberg (J. Biol. Chem. **82**:545, 1929).

11. Laidlaw, G. F., and Blackberg, S. N.: Melanoma Studies: II. A Simple Technique for the Dopa Reaction, Am. J. Path. **8**:491 (Sept.) 1932.

12. Masson, P.: Les naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**:417 (May) 1926.

To investigate a possible infectious etiologic agent—bacteria or virus—a group of three papules were excised under sterile conditions and ground up with an amount of sterile physiologic solution of sodium chloride equal to approximately ten times the volume of the excised skin. One portion of the resulting emulsion was incubated at 37 C. aerobically in broth of p_H 7.6 containing 0.1 per cent dextrose and a 0.2 per cent solution of di-sodium hydrogen phosphate (Na_2HPO_4; 12 H_2O). Another portion was incubated anaerobically at 37 C. in broth of p_H 7.2 to 7.4 containing calves' liver and 0.5 per cent dextrose. There

Fig. 9.—Low magnification of specimen examined on Jan. 2, 1936, showing parenchymatous edema and swelling of the cutis involving vessels and perivascular tissues. Granular necrosis of part of the epidermis, resulting in cavity formation with broken-down cellular elements. The middle portion of the cutis shows granular necrosis of the vessel walls, cellular infiltrate and surrounding cutis framework.

was no growth in either medium at the end of one week. Of a third portion 0.1 cc. was inoculated intradermally into an unaffected area of skin on the patient's forearm and into a corresponding situation in a normal person. Neither the patient nor the control showed any immediate or late reaction to the inoculation.

HISTOLOGIC OBSERVATIONS

Dr. David L. Satenstein [13] examined several biopsy specimens and reported the results as follows:

Biopsy Made on April 3, 1935.—The predominant changes were located in scattered areas of the pars papillaris, extending up to the basal cell layer of the epidermis. Two such areas were noted in the section. The remaining portion of the cutis exhibited practically no notable pathologic changes aside from some

Fig. 10.—High magnification of section shown in figure 9, showing necrosis and cavity formation.

dilatation of the vessels and a few small round cells (lymphocytes) in the perivascular lymph spaces.

The epidermis of the entire section except the portion overlying the affected pars papillaris retained its normal general architecture. In the altered areas the

13. According to Dr. Satenstein the following stains were employed: congo red, sudan IV, hematoxylin and eosin, Roger's nerve stain, methyl violet, dopa and the stains used as a routine for elastic tissue.

basal cell layer was almost completely wanting. The overlying prickle cells were considerably compressed and arranged more or less parallel to the surface; the cell bodies were somewhat indistinct. The granular layer of the entire section consisted of one layer of cells, save in the affected parts, where it was composed of three and four strata. There was a moderate increase in the lamellae of the horn overlying the affected epidermis. There was absence of edema in the epidermis as well as absence of acanthosis; there was no infiltration of any of the contents of the cutis.

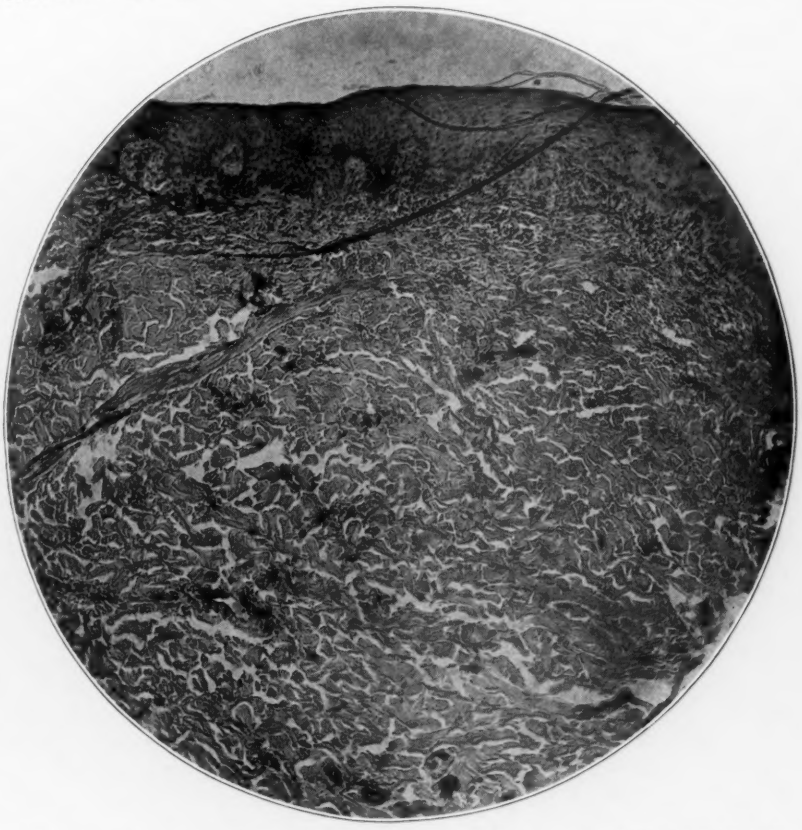

Fig. 11.—Low magnification of specimen examined on April 3, 1935, showing resting stage or end-stage of some previously active process.

In the pars papillaris, involving approximately three papillary zones, there was a fairly dense cellular mass enmeshed with fine scattered connective tissue fibers but nowhere suggestive of a reticulum. The cells in this area were of the connective tissue variety, with large nuclei, some with and some without nucleoli; there were a few large round cells and some flattened fibroblasts. Below this area were a few fibroblasts fading off into the surrounding cutis. In this area there was an absence of blood vessels, of degenerative changes and of plasma and giant cells.

Résumé: The process seemed to depict an end-result or a resting stage of some previously active change. There was nothing in the section to indicate what

the previous picture or process might have been. The impression was that some type of organizing tissue, as is sometimes encountered in the early stages of some of the fibromas, was present.

Biopsy Made on Oct. 2, 1935.—The active process was predominantly in the upper portion of the cutis, the remaining part presenting a moderate interstitial and parenchymatous edema in the deeper layers; otherwise there were no notable changes.

The overlying epidermis was in part acanthotic and in part normal. There was some fusion of the rete pegs and some broadening but no thinning of the subpapillary plates. In the basal zone of some of the rete pegs a slight amount of pigment was present, but this was not a uniform observation. The granular layer was everywhere intact and unchanged. The horny layer showed a moderately finely laminated structure. At the orifice of a sweat duct there was an increased amount of compact horny material, filling the orifice completely. There was no evidence of edema of the epidermis and no disturbance or disorganization of the basal cells, and there was absence of elements from the underlying cutis.

In the upper portion of the cutis all the vessels were to some degree dilated; there was a dilatation of the perivascular lymph spaces, which contained a few cellular elements. An occasional dilated capillary was visible within a papillary body. The lymphatics in the upper portion of the cutis were dilated. The walls of some of the vessels were swollen and somewhat homogeneous, suggesting colloid or hyaline degeneration. The nuclei of the lining endothelium projected into the lumen. Some of the vessels were almost completely occluded. In the perivascular lymph spaces were a few small round cells with deeply stained nuclei, and larger somewhat elongated cells with larger nuclei containing somewhat loose chromatin. There were no plasma cells or giant cells. The surrounding cutis presented a considerable number of scattered fibroblasts. A few chorioplaques were noted high up in the cutis. There was absence of disturbance of the elastic tissue; no evidence of degeneration or necrosis of either the connective tissue or the cellular elements was noted.

Résumé: The process consisted of a moderate exudative inflammatory change which had probably undergone a slow development; it had not advanced to a great extent, remaining superficial and resulting in a degeneration of the vessel walls. The entire picture was not of sufficient intensity to be interpreted as characteristic of any orthodox dermatosis.

Biopsy Made on Nov. 25, 1935 (Osmic Acid Stain).—This section lacked informative material. Minute droplets taking the black dye were scattered throughout parts of the epidermis; scattered larger droplets were seen in the deep layers of the cutis.

Résumé: There was absence of lipoidosis aside from what is normally encountered.

Biopsy Made on Jan. 2, 1936.—The active process extended through the entire cutis as well as into portions of the epidermis. Owing to parenchymatous edema the entire cutis was markedly swollen. The vessels and perivascular tissues were predominantly affected, although other areas of the cutis were involved to a lesser degree. Over one half of the section the overlying epidermis was considerably flattened and somewhat hypertrophied. The central portion of the section, occupying an area of about a half-dozen papillae, exhibited an almost complete granular necrosis of the epidermis resulting in the formation of a cavity containing broken-down cellular elements. In the epidermis surrounding this area there was a considerable degree of degeneration of some of the epidermal cells, causing a loss

of cellular outline. Immediately below this cavity, forming its floor, the cutis showed signs of degenerative changes. The walls of the vessels, especially in the middle and upper portions of the cutis, were swollen and somewhat homogeneous, and contained numerous broken-down cellular elements; the lumens in some were completely occluded; in others they were still visible, being lined with swollen endothelium. In the perivascular lymph zones were closely packed broken-down cells. Similar cellular detritus was noted lying between bundles of swollen connective tissue in the perivascular zones. Some of these bundles were finely granular.

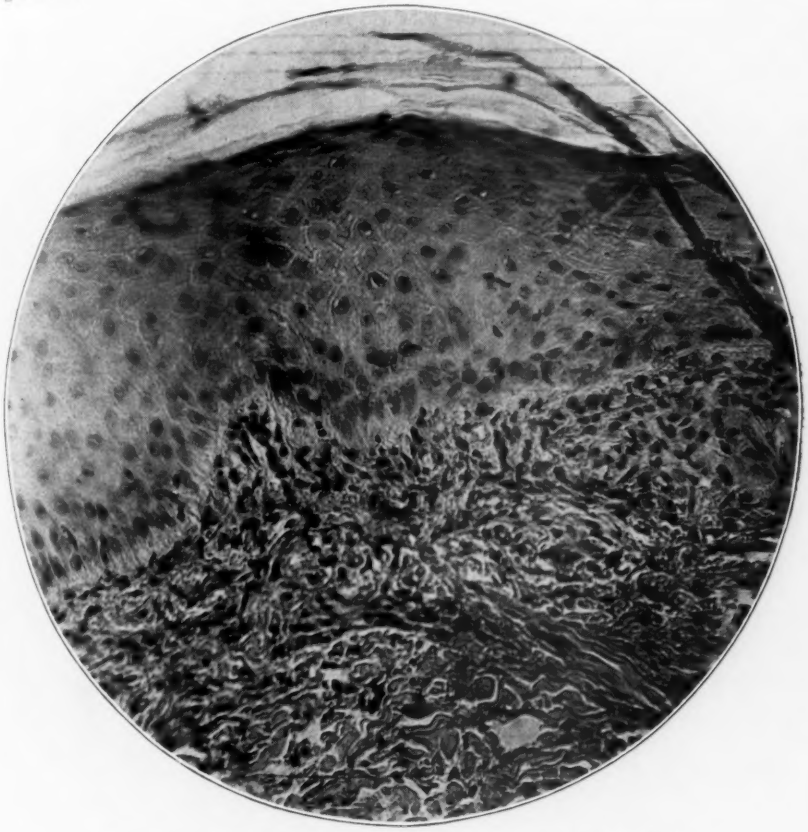

Fig. 12.—High magnification of section shown in figure 11.

In the deeper portions of the cutis some proliferation of fibroblasts was seen. In the subepidermal zone the cellular infiltration was composed predominantly of lymphocytes; here the greater portion of the cutis was homogeneous and had lost its characteristic structure.

The sweat glands exhibited a high grade of so-called cloudy swelling of the lining cells with some hyaline degeneration of their connective tissue coats. In one of the sebaceous glands fragmentation of the cells was noted and considerable cellular detritus surrounded the gland.

Résumé: In this section the entire histologic picture was one of rather profound degeneration and disintegration of the walls of the vessels, the cellular

infiltrate and the framework of the cutis. It was suggestive of a necrotic dermatitis involving especially the vascular elements.

The section did not exhibit changes tending to indicate etiologic or pathogenic factors or to correlate the histologic observations with the clinical-morphologic picture.

Summary of Histologic Observations.—From the histologic study of four pieces of tissue removed from different parts of the body and examined, respectively, on April 3, 1935; Oct. 2, 1935; Nov. 25, 1935, and Jan. 2, 1936, it is not possible in the light of the chronologic sequence indicated to visualize the pathologic process. However, a rearrangement of the specimens makes such a visualization feasible.

The specimen examined on Oct. 2, 1935, indicated the early stage of the pathologic process, namely, one consisting of an exudative inflammatory reaction in the upper portion of the cutis associated with a degeneration of the vessel walls but as yet no necrosis of any of the tissues or of infiltrative elements.

The last section, examined on Jan. 2, 1936, evidently showed the process at its height, as indicated by intense degeneration and disintegration of tissue and of cellular infiltrate as well.

The first section, examined on April 3, 1935, presented the final stage of the process, i. e., the deposition of connective tissue cells—possibly organizing tissue—replacing the parts which had broken down.

There were no changes in the specimens which would lead one to link the pathologic picture with any form of the so-called lichens.

The process was evidently one in which vascular disease associated with degenerative changes was the predominant morbid alteration.

SUMMARY AND CONCLUSIONS

By a process of elimination the compilation and perusal of the cases recorded as instances of lichen ruber moniliformis leaves only two instances in which microscopic examination definitely excludes lichen planus, namely, Kaposi's and our case. The similarity of clinical manifestations in these two cases and the obvious dissimilarity of the picture to that in cases in which microscopic examination revealed lichen planus seem to support the contention of the critics who regard the original "lichen ruber moniliformis" not only as a dermatosis unrelated to lichen planus but possibly as one which might prove to be a disease sui generis. The histologic changes in our case would at least lead one to accept this point of view.

The points of resemblance between Kaposi's and our case may be summed up as follows: There is a close parallelism in the distribution of the lesions, their morphologic features, their multiformity, their variations in color, size and arrangement, the absence of marks of scratching, the chronicity, the similarity of some elements to papules of lichen planus and finally, the lack of discoverable etiologic and pathogenetic features. On the other hand, the dermatosis in Kaposi's case differs from that in ours in that the longitudinal banded keloid-like formations on the neck and extremities were far more pronounced and much more

prominent in his case than in ours; in his case there were central depressions in some of the papular elements, lesions of the labial and buccal mucosa, a retiform design of papular chains on the thighs, longitudinal bands on the lower portion of the abdomen and a scattering of pigmented puncta in the midst of the other lesions. Judging from his description the buccal manifestations possessed none of the diagnostic features of lichen planus. In neither case was the glans penis involved.

Regarded from a broad point of view it might be assumed that the dermatosis in Kaposi's case was a manifestation of a much further advanced phase of development and evolution than that which obtained in our patient. This point of view is, of course, a purely conjectural one, especially when one considers the great discrepancies in the respective microscopic structural features.

We are concerned with a dermatosis the character of which appears to be in certain respects unique. Since dermatologic literature abounds in new and often confusing names, it behooves one to restrain the creative impulse and to avoid as much as possible further derangements of nomenclature. Nevertheless, a different name seems desirable, and the new name should preferably be one which would serve to maintain a plausible harmony with the original. Taking into consideration the clinical similarity of the dermatosis exhibited by our patient to that described by Kaposi, its nonrelation to lichen planus, the lack of etiologic and pathogenic clues to its identity and, finally, the desirability of not insulating it from Kaposi's designation, we have selected for the dermatosis the neutral name morbus moniliformis lichenoides.

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ABSTRACT OF DISCUSSION

DR. F. M. JACOB, Pitttsburgh: As the authors have stated, a review of the literature, particularly of the textbooks, shows the general belief to be that lesions of lichen ruber moniliformis are not often found in association with lichen planus. This is easily understood because clinically lesions that are found occasionally in association with lichen planus are similar to the individual lesions described in this case.

I recently observed a case of what appeared to be clinically a beginning of lichen ruber moniliformis; there were waxy yellowish lesions about 3 mm. in diameter on the arms and wrists, deep-seated domed lesions that had no resemblance to clinical lichen planus but histologically showed a definite picture of lichen planus and no characteristics that could be compared to the ones in Dr. Wise and Dr. Rein's case.

There are several diseases previously described that have some similarities to this, namely, some of the diseases that appear under the description of scleroderma, lichen sclerosus et atrophicus, lichen morphoeicus atrophicus and dermatitis lichenoides chronica atrophicans. Montgomery and Ormsby differentiated between white spot disease and lichen sclerosus some time ago, and in their cases of lichen

sclerosus there were some histologic features that were similar to those in the case reported by Dr. Wise and Dr. Rein. Wise and Shelmire in a paper on dermatitis lichenoides chronica atrophicans also showed some histologic similarities to the disorder under consideration. In writing both papers Dr. Wise was able to stress the differential points.

Satenstein in the same way has stressed the differential points between lichen ruber moniliformis and these other diseases with particular regard to the pigmentation, the formation of reticulum, the character of the exudate and the final connective tissue reaction which was present in Dr. Wise and Dr. Rein's case.

The one particular feature, however, that is found to be similar in all the aforementioned conditions is the changes in the deeper blood vessels, consisting first of swelling and later of proliferation of the endothelial lining of the blood vessels, leading to occlusion of these vessels. This suggests some deep-seated toxic process that may be similar in all of these conditions.

In spite of the fact that the nomenclature is rather overcrowded, I think it is not amiss to give this disease the descriptive name Dr. Wise and Dr. Rein have suggested in order that it be differentiated from lichen planus until its nature is ascertained.

Dr. Hamilton Montgomery, Rochester, Minn.: Dr. Wise and Dr. Rein are to be complimented on the thoroughness with which they studied their case, especially as to the ruling out of such changes as deposition of lipoid and amyloid. The histologic picture is unlike any I have seen before. The disorder obviously is not lichen planus and does not fit in with the picture of scleroderma, lichen sclerosus et atrophicus or morphoea guttata. It is difficult to explain the necrosis present in the fully developed lesion, especially since, as I understand, it was not apparent clinically.

I want to call attention to Dr. Ormsby's case, in which, I understand, the disorder has persisted over a period of about twenty years and has not responded to treatment. The latter is true of Dr. Wise and Dr. Rein's case. This, together with the unusual picture, suggests that the condition may be a nevoid vascular disturbance of some kind, the term nevus being used in the broad sense.

Dr. L. H. Winer, Minneapolis, Minn.: I did not think that the picture in the slide shown resembled lichen planus at all, and I agree with Dr. Montgomery that it does not resemble a lichenoid scleroderma. Still, at the termination of the process the lesions healed with relative increase of the connective tissue, and therefore my impression is that this condition eventually will be more closely related to the sclerodermas or the tense atrophies than to lichen planus.

Dr. Fred D. Weidman, Philadelphia: This paper is of value from two points of view: (1) from the clinical one involvnig nomenclature, with its bearing on erudite dermatologic diagnosis and general clinical dermatology, and (2) in relation to the etiology. However, I think that the more valuable feature of this presentation is in relation to the latter aspect; the clinical circumstance that these nodules, at least in part, tend to extend in strands makes one think of some particular anatomic structure in the skin, and since these lesions appear most conspicuously at the flexures of the elbows, the lines of fibrous overgrowth that appear in connection with stress and strain seem to be important.

Thus, it is well known (English authors discuss this more than American authors) that among the various expressions of rheumatism there is a lesion which is called fibrositis; it is a nonspecific type of fibrous reaction. After joining up what has been shown here clinically, namely, the pattern of the lesions on the skin, with what has been demonstrated histologically, I think that attention ought to turn toward the possibility of a diffuse generalized toxic state which is analo-

gous to rheumatism. I suggest as the most promising line for studies in the etiology of this disease cultures of the blood and examination of the economy at large for foci of infection.

Such a wealth of information would not have been available had Dr. Wise and Dr. Rein limited their study to but one or two biopsies. But eleven biopsies were made. Only in that way were the authors able to find one lesion which fortunately happened to show the acute and more informative phases of the fundamental pathologic process.

Dr. Charles R. Rein, New York: I wish to call attention to the two cases reported in this country, one by Fox and the other by Hyde and Ormsby, which were the only ones in which the disorder closely resembled that in our case. Unfortunately, however, tissue for microscopic examination was not obtained in these cases.

Regarding Dr. Weidman's discussion, I wish to state that our patient was carefully examined for foci of infection; the results of the various examinations gave essentially negative results.

PSEUDO-ACHROMIA OF TINEA VERSICOLOR

CLINICAL AND EXPERIMENTAL STUDIES AND OBSERVATIONS ON THE USE OF FILTERED ULTRAVIOLET RAYS (WOOD FILTER)

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A patient with tinea versicolor not uncommonly exhibits during the summer or autumn light-colored (apparently depigmented) areas on the surfaces of skin exposed to sunlight. These areas usually appear suddenly, after sunburn followed by peeling, although a history of a visible reaction is not always obtained. The patches occupy the sites of lesions of tinea versicolor, being irregular and of various size, and appear chiefly on the trunk. Their color is not the dead white of vitiligo, although in contrast to the surrounding skin, especially in persons of dark complexion, they may be mistaken for that disease. Other areas of skin on the covered parts of the body are usually found to match the color of the achromic-appearing spots. There is no increase of pigment at the periphery of the lesions. A scarcely perceptible scaling may be noted. Sometimes the condition appears year after year, becoming less noticeable during the winter and reappearing during the summer. This manifestation of tinea versicolor was first described by Ehrmann [1] and has been studied by Wertheim,[2] Kistiakovsky,[3] Gougerot, Joyeux and Arnaudet,[4] Artom,[5] del Vivo,[6] Ruete [7] and others.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, and the New York Hospital and Department of Medicine (Dermatology), Cornell University Medical College.

1. Ehrmann, cited by Wertheim.[2]

2. Wertheim, L.: Ueber Lichtwirkung und Leukoderma bei Pityriasis versicolor, Dermat. Ztschr. **38**:343 (June) 1923.

3. Kistiakovsky, E. V.: (*a*) Pityriasis Versicolor and Ultraviolet Rays, Arch. Dermat. & Syph. **15**:685 (June) 1927; (*b*) L'achromie, qui apparaît sous l'action des rayons ultra-violets du soleil sur le pityriasis versicolor, est-elle parasitaire ou post-parasitaire? Ann. de dermat. et syph. **1**:1264 (Dec.) 1930.

4. Gougerot, Joyeux and Arnaudet: Un cas d'achromie parasitaire nord africain, Bull. Soc. franç. de dermat. et syph. **37**:110 (Jan.) 1930.

5. Artom, M.: Contributo allo studio della pityriasis versicolor acromizzante, Gior. ital. di dermat. e sif. **71**:1945 (Dec.) 1930.

6. del Vivo, G.: Sulla cosi detta pityriasis versicolor acromizzante, Rinasc. med. **9**:270 (June 15) 1932.

7. Ruete, A. E.: Zur Frage der depigmentierenden Pityriasis versicolor, Dermat. Wchnschr. **96**:333 (March 11) 1933.

The light-colored areas do not, as a rule, become tanned after further exposure to ultraviolet radiation; on the contrary, they become more and more noticeable owing to the increase of pigment in the surrounding normal skin. The condition has been said to occur in the skin of Negroes in association with the development of definite depigmentation. The development of lesions on covered parts of the body which have not been sunburned has been reported. Furthermore, the dopa reaction has demonstrated that the pigment-forming oxidase may be affected. For these reasons it has been suggested that the light-colored areas may be due to a toxic action of the fungi on the pigment of the skin resulting in an inhibition or destruction of the pigmentary powers of the skin. The rôle of the sun in activating the fungi is not clear. The explanation for the persistence of the light-colored areas, namely, that the fungi in the lesions of tinea versicolor act as a mat or filter to prevent the ultraviolet rays from the sun from passing through, is held by many observers.

DIFFERENTIAL DIAGNOSIS

Certain other diseases with similar clinical pictures must be considered in a differential diagnosis from the pseudo-achromia of tinea versicolor. Among these may be mentioned *achromie parasitaire à récrudescence estivale* (Jeanselme), achromia parasitaria (Pardo-Castello and Dominguez), tinea flava (Castellani), the endemic vitiligo of Turkestan (Minch) and pinta in the quiescent stage. Besides post-eruptional depigmentations, the condition may also be confused with syphilitic leukoderma and with ordinary vitiligo.

1. *Achromie parasitaire à recrudescence estivale.*—From the published description [8] it appears that this is the same disease as the one under consideration in this paper.

2. *Achromia parasitaria.*—It is difficult to fit together the varied symptoms in the syndrome which Pardo-Castello and Dominguez [9] described. In some cases of achromia parasitaria irregular dirty white macules and patches with slight inflammation, which are scaly and somewhat itchy, are present on the face and neck. In other cases the eruption is generalized, no inflammatory symptoms are present and the disorder simulates the pseudo-achromia of tinea versicolor. On one of the illustrations in the article by Pardo-Castello and Dominguez are shown lesions on the trunk which are suggestive of the disease under discussion in this report. In both disorders the scaling in the early macules is white and furfuraceous, and the older lesions are devoid of scales.

8. Jeanselme: Cours de dermatologie exotique: Achromie parasitaire de la face et du cou, à recrudescence estivale, Paris, Masson & Cie, 1904, p. 239.

9. Pardo-Castello, V., and Dominguez, M.: Achromia Parasitaria, Arch. Dermat. & Syph. **9**:82 (Jan.) 1924.

There is no increase of pigment at the edges. The mucous membranes, hair and nails are not affected. In the series reported by Pardo-Castello and Dominguez there were four cases in which the disorder was generalized, the palms and soles being free. Aspergillus was cultured in six of thirty-six cases and was considered a possible cause of the disease. No mention was made of the examination of scales in potassium hydroxide for the presence of Microsporon furfur. In a later communication Pardo-Castello [10] expressed his belief that the same clinical picture might be found in patients of different races and in persons residing in different countries, that it might affect different types of persons and that it might be caused by a variety of organisms. He did not believe that the rays of the sun play any part in the etiology. Further investigative work appears necessary to clarify the picture.

3. *Tinea Flava or Tinea Versicolor Tropicalis.*—Castellani [11] stated that this condition is identical with achromia parasitaria (Pardo-Castello and Dominguez). The fungus responsible cannot be distinguished from M. furfur in potassium hydroxide preparations and, like that organism, is nonculturable. Castellani [12] differentiated tinea flava from tinea versicolor as it occurs in the temperate zones by the following points: (1) tinea flava begins in childhood and may persist during life; (2) it usually affects the exposed parts of the body; (3) cure is difficult, and (4) the fungus seems to have a marked depigmentary action.

4. *Endemic Vitiligo of Turkestan.*—According to Kistiakovsky,[3a] who has observed the disease, there is no difference between this disorder and vitiligo.

5. *Pinta.*—When this condition is observed early, the characteristic hues of the affected skin in no way suggest tinea versicolor. Later, when vitiliginous areas are present, the differentiation may be more difficult. The disease causes coarse scales, the affected skin is infiltrated, occasional fissuring is noted and loss of hair is usual. When extensively involved, the skin presents an odd piebald appearance.

6. *Syphilitic Leukoderma.*—This condition is seen almost exclusively in women. The lesions are commonly symmetrically located on the sides of the neck, are oval or irregularly shaped and vary from the size of a split pea to that of a dime. Concomitant hyperpigmentation is some-

10. Pardo-Castello, V.: Achromia Parasitaria: Its True Nature and Etiology, Arch Dermat. & Syph. **25**:785 (May) 1932.

11. Castellani, A.: Fungi and Fungous Diseases, Arch. Dermat. & Syph. **17**: 194 (Feb.) 1928.

12. Castellani, A.: A Case of Pityriasis Versicolor Tropicalis, Brit. J. Dermat. **47**:484 (Nov.) 1935.

times noted. No scaling is present. Other evidence of syphilis may usually be detected, including a positive serologic reaction.

7. *Vitiligo.*—The irregular, asymmetrical, snow-white patches, affecting by preference the face, hands, forearms and male genitalia and showing hyperpigmented edges, should not often prove difficult to differentiate. No scaling is present. The appearance of vitiliginous skin when observed under filtered ultraviolet rays is characteristic, presenting a fluorescing, glistening white color.

8. *Posteruptional Depigmentations.*—Seemingly-depigmented areas may be noted at the former sites of syphilitic, psoriatic and other cutaneous lesions. Without any history of a preceding eruption the differential diagnosis may be difficult.

Comment.—Since cases occur in which a clinical diagnosis may be impossible, it is considered not only desirable but necessary to make a positive diagnosis in all cases of pseudo-achromia due to tinea versicolor by means of microscopic studies reenforced by observations with filtered ultraviolet rays.

REVIEW OF RECENT LITERATURE

Kistiakovsky [3a] thought that in many of Pardo-Castello's patients, especially in those with lesions on the back, the picture resembled that of pseudo-achromia of tinea versicolor in patients he had observed. He ascribed the light coloration of the skin to a mechanical screening of the skin underlying the patch of tinea versicolor and pointed out that M. furfur contains a yellowish pigment which strongly refracts light. Because of this property of the organism parts of the skin covered by fungus were not sunburned. He did not agree with Stein, who thought that a special kind of M. furfur was responsible for the condition. Gougerot, Joyeux and Arnaudet [4] and Artom [5] considered the light areas to be a true achromia and not pseudo-achromia due to the contrast between the normal and the surrounding skin. Kistiakovsky,[3b] in a later report, reiterated the view which he had expressed earlier and stated that in all parasitic diseases with an achromic aspect the mechanism of origin is physical and not biologic. Del Vivo [6] reported a case of a disorder which he considered pseudo-achromic. In commenting on this report, Wise and Sulzberger [13] stated that in certain cases of tinea versicolor it is likely that there is a true depigmentation of the skin. They based their belief on several cases in Negroes in which they saw lighter patches of skin become much lighter and contain less pigment than the normal, not sunburned, areas. Ruete [7] expressed the belief that the depigmentation is the result of a biologic phenomenon. In the case he reported the patient had typical tinea versicolor. The brown

13. Wise, F., and Sulzberger, M. B.: The Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1932, p. 29.

spots turned white but became brown again in the winter. The next summer they again turned white. In a section it was demonstrated that pigment was absent below the areas infected with the fungus. Sections stained by Gram's method and the dopa reaction pointed to a true depigmentation. Cases of apparent achromia in patients with tinea versicolor have been reported in the United States by Fox,[14] MacKee,[15] Throne,[16] Barney,[17] Lewis [18] and Bechet.[19]

PERSONAL OBSERVATIONS

We have studied fourteen cases [20] of tinea versicolor in which an apparent depigmentation was noted. Repeated examinations for fungi combined with observation of the patients under filtered ultraviolet rays revealed that organisms were frequently present in these light-colored patches. Treatment was continued until no fungi could be demonstrated. Ultraviolet radiation was then given, resulting in an increase of color in the patches.

CASE 1.—S. R., a blond woman aged 20, single, an embroidery worker, was presented before the Section of Dermatology and Syphilis of the New York Academy of Medicine in November 1934.[18] Patchy areas of apparent depigmentation on the chest and arms corresponded in color to that of the face and neck. A typical brownish patch of tinea versicolor was present on the back. M. furfur was found in scrapings from the lighter areas on the arms and from the brown area on the back. Topical treatment consisting of application of a saturated solution of sodium thiosulfate was continued for three weeks, until there was no evidence of fungi. The patient then received several treatments with artificial sunlight, and within a month pigment had increased in all the pseudo-achromic areas.

CASE 2.—A. F., a woman aged 27, a switchboard operator, showed typical patches of tinea versicolor and numerous areas of apparent depigmentation varying in size on the upper portion of the back. Scaling was noted in these lighter areas. Light brown fluorescence was noted in both the lighter and the darker patches when the areas were examined under filtered ultraviolet rays. M. furfur

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14. Fox, H.: Pityriasis Versicolor Followed by Apparent Depigmentation, Arch. Dermat. & Syph. **15**:751 (June) 1927.

15. MacKee, G. M., in discussion on Fox.[14]

16. Throne, B.: Achromia Cutis Postparasitaria, Arch. Dermat. & Syph. **18**: 146 (July) 1928.

17. Barney, R. E.: Pseudo-Achromia Postparasitaria—Tinea Versicolor, Arch. Dermat. & Syph. **25**:1167 (June) 1932.

18. Lewis, G. M.: Tinea Versicolor (White), Arch. Dermat. & Syph. **31**:911 (June) 1935.

19. Bechet, P.: Vitiligo? Tinea Versicolor? Arch. Dermat. & Syph. **32**:960 (Dec.) 1935.

20. Twelve cases were observed in the service of Dr. Fred Wise in the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, and two cases were observed in private practice.

was demonstrated in scrapings taken from both types of patches. Local treatment was continued for one month. The patient then received three erythema doses of ultraviolet rays at weekly intervals, and the normal color of her skin returned.

CASE 3.—R. W., a man aged 23, married, a clerk, had whitish patches of various sizes on his trunk and several typical areas of tinea versicolor on the sides of his neck and trunk. Examination revealed fungi in the brown areas; no fungus was found in the whitish patches. Topical treatment was instituted for three weeks. At the end of that period examination for tinea gave negative results in all the areas. Two treatments with ultraviolet rays brought back

Fig. 1.—Apparent depigmentation at the sites of lesions of tinea versicolor following an acute sunburn. M. furfur was found in scales from several lesions.

some color in the apparently depigmented areas. The patient was not observed further.

CASE 4.—V. S., a woman aged 21, single, had numerous coin-sized roundish "depigmented" patches on the upper portion of the back; these were said to have been present for several months. No brown patches were noted. Examination of scrapings from the lighter areas revealed M. furfur. Local treatment was instituted, and four weeks later the examination for tinea gave negative results. One treatment with ultraviolet rays was given, but the result was not ascertained.

The development of pseudo-achromic patches was observed to appear at the sites of tinea versicolor. These light areas had not been present when the patient was previously seen.

CASE 5.—J. G., a woman aged 30, when first seen had scaly fawn-colored patches on her back. The examination revealed M. furfur. The patient did not use the local treatment prescribed. When she was observed two weeks later, after she had suffered acute sunburn several times, the sites of the eruption showed less pigmentation than the surrounding skin. The color in these areas was not vitiliginous but rather that of normal skin not reached by the sun. Scaling was still present in the areas, and the examination for fungi and the fluorescence test gave positive results. The patient did not return for further study.

Fig. 2.—Characteristic light-colored areas. M. furfur was demonstrated in scales from these lesions.

The observation of tinea versicolor under filtered ultraviolet rays is useful not only as a diagnostic aid but also in determining the extent of the eruption. Lesions not visible in ordinary daylight fluoresce with the golden brown color typical of the ordinary patches.

CASE 6.—P. B., a woman aged 23, single, a clerk, had typical patches of tinea versicolor on her chest. Under filtered ultraviolet rays additional fluorescent areas (not visible in daylight) were noted on the back of the neck, across the shoulders and on the outer aspect of the anterior portion of the forearm and arm. No local treatment was prescribed. The patient received sufficient sunburn at a

beach so that all areas of tinea versicolor, the visible as well as the invisible ones, were exfoliated. One week later there was a definite lightness at the sites of the patches of tinea versicolor, as compared to the surrounding skin. M. furfur could still be demonstrated, and fluorescence was still noted. Topical treatment was instituted, and in two weeks no evidence of fungi could be detected. Further exposure to the sun then resulted in an increase of pigment in the light-colored patches.

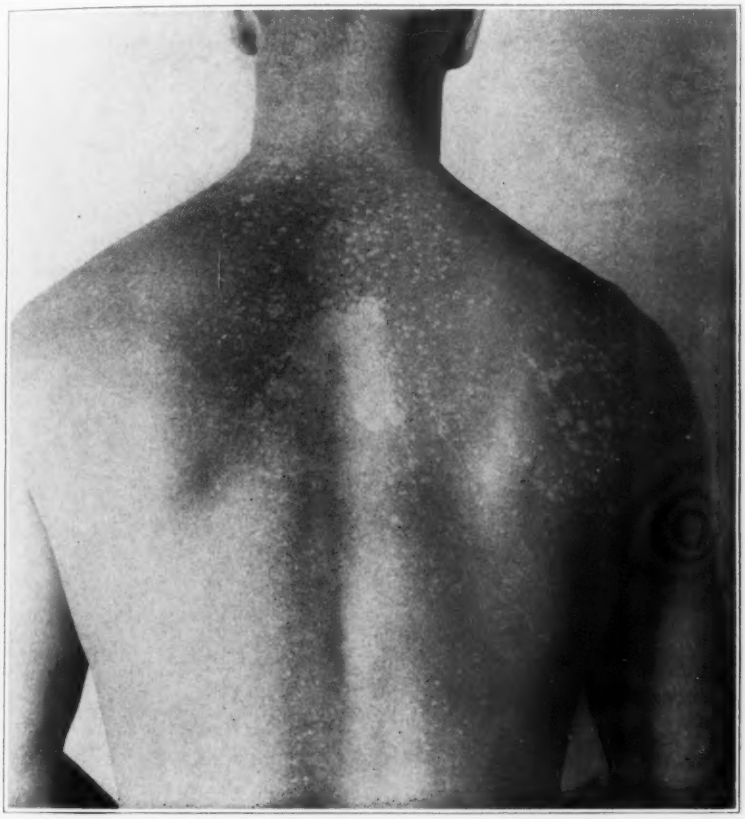

Fig. 3.—Small and large areas of pseudo-achromia, which showed the fluorescence characteristic of tinea versicolor when examined under ultraviolet rays and from which M. furfur was recovered.

CASE 7.—G. K., a woman aged 28, single, a dress finisher, had a typical eruption of tinea versicolor on the trunk for over two years. Her skin had not been exposed to the sun, and there were no areas of apparent depigmentation. The examination for fungi revealed M. furfur. Examination with filtered ultraviolet rays disclosed several additional areas not noted in ordinary light (fig. 4). The patient was not observed further.

MYCOLOGIC EXAMINATION OF THE PSEUDO-ACHROMIC AREAS

The microscopic appearance of the fungi present in the light-colored areas varied somewhat from the picture in a typical patch of tinea versicolor. Few spores were noted, and there was no appreciable grouping. The filaments were few and consisted of short rods.

USE OF FILTERED ULTRAVIOLET RAYS

The well known golden yellow or brown fluorescence noted when lesions of tinea versicolor are examined with filtered ultraviolet rays

Fig. 4 (case 7).—Photograph of lesions of tinea versicolor as seen under filtered ultraviolet ray and outlined in ink. These lesions were not visible in ordinary daylight.

has made such examination a useful diagnostic procedure for many years. The color has varied in different cases from a light brown or yellowish color to a dark brown. The difference in color appears to depend on the amount of pigment in the patch, so that in lesions of tinea versicolor which are quite dark the fluorescent color is also dark. The production of this pigment appears to have some relation to stimulation due to the sun's rays, since the patches may be so light as to be almost invisible during the winter and assume a much darker hue during the period of exposure to insolation. The light-colored areas, which may

be almost invisible to the naked eye, fluoresce brilliantly. It is suggested that the frequent recurrence of tinea versicolor may be due, in part at least, to these practically invisible areas, which provide a focus for dissemination during the summer. So far as the light-colored (pseudo-achromic) areas are concerned, a light brown fluorescence is noted under filtered ultraviolet rays as long as fungi may be demonstrated in scrapings from these areas. When no further fungi can be detected, the color is dull white (in contrast to the brilliant white of vitiligo). The distribution of tinea versicolor may be quickly and accurately determined in any given case by examining the patient with filtered ultraviolet rays. It was found that lesions of tinea versicolor usually occurred on the areas of the trunk on which seborrhea usually develops, but the back of the neck and the extensor surfaces of the arms were not uncommon sites. In two instances lesions were present on the face, and in one lesions were observed in the pubic region. In no case was a patch of tinea versicolor noted on the lower extremities. The scalp was similarly free.

NATURE OF THE LIGHT-COLORED (PSEUDO-ACHROMIC) AREAS

It appears logical to conclude that in the fourteen cases of tinea versicolor which we studied and in which a light-colored area of skin was also present a mechanical and not a biologic factor was responsible for the light color. In some instances, particularly in the case of patients with dark skin, the light-colored areas appeared achromic. Further observation usually made it possible to match the color of the light-colored patches with other areas of the patient's skin which had not been reached by the sun's rays. It is assumed that the persistence of the apparent achromia is due to the continued presence of fungi on the surface of the light-colored patches. When these fungi were destroyed and ultraviolet radiation was administered an increase of pigmentation was noted in the patches.

The nature of the pseudo-achromia was further investigated by the following methods:

1. Sections of skin from the light-colored areas were removed from two patients and prepared for examination of pigment. Tests made according to the technic of Becker, Praver and Thatcher [21] showed normal pigment to be present in the basal layer of the epidermis, and chromatophores were also demonstrated in the cutis.

2. Scales from lesions of psoriasis, pityriasis rosea and tinea versicolor were collected separately. Equal amounts by weight of the three specimens were then applied to equal areas of skin, and erythema doses of ultraviolet radiation

21. Becker, S. W.; Praver, L. L., and Thatcher, H.: An Improved (Paraffin Section) Method for the Dopa Reaction, Arch. Dermat. & Syph. **31**:190 (Feb.) 1935.

were administered to these areas. Absolute protection was not obtained in any of the three areas, but there was a noticeable degree of protection in all. The areas covered with scales of tinea versicolor showed less erythema and subsequent pigmentation than the areas covered with the other two kinds of scales.

3. Unsuccessful attempts were made to extract fluorescent material from scales appearing on lesions of tinea versicolor. The solvents used were alcohol, ether, acetone and physiologic solution of sodium chloride. The scales were allowed to stand in the solvents, being occasionally shaken for over a week. In another unsuccessful attempt, a Soxhlet apparatus was used. It is not known whether the fluorescent material was insoluble in the solvents used or whether the amount of fluorescent material present in the scales was too small to be appreciably noted in the volume of solvent.

4. Fluorescent material from Microsporon lanosum and Trichophyton gypseum was removed by shaking cultural growths of these organisms with acetone. The solution was allowed to concentrate and applied to test areas of skin and left to dry. An erythema dose of artificial ultraviolet radiation was then administered. A definite screening effect was obtained at the site of application, evidenced by less redness and subsequent pigmentation than in the surrounding skin.

These experiments appear to offer a logical explanation for the pseudo-achromia. The theory of biologic inhibition or destruction of pigment is further discountenanced by analogy when one recalls that thousands of injections of fungous extracts have been administered in the form of injections of trichophytin and that—as far as we know—no pigmentary changes have been reported to have appeared at the site of injection. If M. furfur were culturable, this point could quickly be settled. It appears important that M. furfur be demonstrated in the scales from the lesion of tinea versicolor from which a section is removed for histologic studies of pigment just before material is removed for biopsy. There is no reason why a patient with tinea versicolor should not also suffer from vitiligo.

SUMMARY

In fourteen patients with tinea versicolor, light-colored patches developed when the affected skin became sunburned. Further exposure to the sun's rays did not result in erythema or in tanning in the light-colored areas, but, on the contrary, they became more prominent owing to an increase in pigment in the surrounding skin. Examination of scales from these areas revealed fungi which were considered to be atypical M. furfur. Treatment was carried out for several weeks until no fungi could be demonstrated. Tanning of the skin in the light-colored areas could then be brought about by ultraviolet irradiation. Evidence is offered in favor of the theory that a purely mechanical factor is responsible for the light-colored areas as against the theory of biologic interference with the pigmentary mechanism of the skin. This evidence included (1) an examination for pigment by means of

the dopa reaction, which revealed a normal amount of pigment in the skin, (2) a comparison of scales from lesions of psoriasis, pityriasis rosea and tinea versicolor, which showed that scales from lesions of tinea versicolor protected the skin from ultraviolet rays to a greater degree than scales from lesions of either of the other conditions, and (3) attempts to extract fluorescent material from these scales, which were unsuccessful while, on the other hand, attempts to extract fluorescent material from other fungi in culture proved successful and the extracted material was found to have a screening effect when ultraviolet radiation was administered.

The characteristic fluorescence of the lesions of tinea versicolor as seen under filtered ultraviolet rays is of value not only in arriving at a diagnosis but also in determining the extent of the eruption, since lesions not visible in ordinary light can thus be detected. While the lesions of tinea versicolor were usually confined to the trunk, patches were noted in several instances on the back of the neck and on the extensor surfaces of the arms. Failure to treat all involved skin may explain the frequent recurrences noted in this disease.

200 West Fifty-Ninth Street.

SMALL RADIUM NEEDLES IN TREATMENT OF MALIGNANT CUTANEOUS TUMORS

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AND
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Recent advances in the radiation therapy of cancer have not been fully recognized by American dermatologists, nor have the therapeutic advantages offered by the newer methods of irradiation been widely utilized by them; radiologists, however, have readily adopted these new procedures. Dermatologists have many advantages in their superior ability to diagnose cutaneous lesions and in their more accurate knowledge of cutaneous reactions, and they should adopt these new measures to maintain their therapeutic superiority in the treatment of cutaneous malignant tumors.

Régaud [1] and his associates at the Radium Institute in Paris have proved, both experimentally and clinically, that to obtain the most effective result from irradiation in treating malignant lesions it is necessary to prolong the radiation time. This necessitates diminution of the strength of radium needles when interstitial methods are used or increase of the distance between the source of gamma rays and the area to be treated when surface radiation is employed. More homogeneous irradiation of the mass to be treated may be obtained by the use of multiple, equally spaced points of radiant energy.

Régaud obtained sterilization of a ram's testis by prolonged irradiation with feeble doses of gamma rays, although he failed to do so by using five times the dose for a shorter period. From this experiment he concluded that the cells were more radioresistant at certain stages of their life cycle than at others. He stated: "In the center of the ram's testicle, 15 dose units of heavily filtered emanations, acting during a few hours only, produced a central necrosis without sterilizing the outer parts of the organ; in remarkable contrast, 3 dose units acting during 15 days, have effected complete sterilization, but without necrosis." The application of this observation to the treatment of

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From the Department of Dermatology, Baylor Medical College.

Read at the Fifty-Ninth Annual Meeting of the American Dermatological Association, Inc., Swampscott, Mass., June 6, 1936.

1. Régaud, C.: Some Biologic Aspects of the Radiation Therapy of Cancer, Am. J. Roentgenol. **12**:97 (Aug.) 1924; Radium Therapy of Cancer at the Radium Institute of Paris, ibid. **21**:1 (Jan.) 1929.

cancer has given greatly improved results, and some types of squamous cell carcinoma which were previously considered as radioresistant have proved to be radiosensitive. The radiation treatment of cancer should utilize this selective action of the rays instead of their diffuse caustic effect.

These new principles were first used by Régaud, who employed multiple radium tubes at increased distance. This biologic principle was then adapted to interstitial therapy by Cade.[2] The work was further developed by Evans and Cade and by Birkett, British radiotherapeutists; in this country it was carried out by Kaplan,[3] Lenz,[4] Martin,[5] Soiland,[6] Treves,[7] Cole and Driver [8] and others. Similar biologic principles have been utilized by Coutard [9] in his plan for a multiple dose of heavily filtered roentgen radiation, and J. M. Martin and C. L. Martin [10] have described a modification of Coutard's technic. With the addition of filtration, these methods are but revivals of the broken dose method of roentgen irradiation advocated by Pusey [11] more than thirty years ago.

In this communication we propose to deal with the technic and dosage in the use of platinum iridium needles containing small amounts

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2. Cade, S.: (*a*) Radium Therapy of Cancer of the Buccal Cavity, Lancet **1**:8 (Jan. 5) 1929; (*b*) Radium Therapy of Cancer, New York, William Wood & Company, 1929.

3. Kaplan, I.: Radium Treatment of Cancer of the Breast, Am. J. Roentgenol. **25**:250 (Feb.) 1931.

4. Lenz, M.: Curie Therapy of Epidermoid Carcinoma of the Intra-Oral Group as Carried Out at the Institute of Paris, Am. J. Roentgenol. **15**:216 (March) 1926; Radium Therapy of Cancer, Arch. Phys. Therapy **14**:393 (July) 1933.

5. Martin, C. L.: Small Radium Needles Versus Radon Implants, Am. J. Roentgenol. **27**:240 (Feb.) 1932.

6. Soiland, A.: Diagnosis and Treatment of Carcinoma of the Breast, Southwestern Med. **17**:153 (May) 1933.

7. Treves, N.: A Small Platinum Needle Designed for the Use of Various Strengths of Radium Element Interstitially, Am. J. Roentgenol. **33**:537 (April) 1935.

8. Cole, H. N., and Driver, J. R.: Radium Dosage and Technic in Carcinoma of the Skin, Am. J. Roentgenol. **33**:682 (May) 1935.

9. Coutard, H.: Roentgen Therapy of Epitheliomas of the Tonsillar Region, Hypopharynx and Larynx from 1920 to 1926, Am. J. Roentgenol. **27**:313 (Sept.) 1932.

10. Martin, J. M., and Martin, C. L.: Modified "Coutard" Roentgen Therapy, J. A. M. A. **104**:605 (Feb. 23) 1935.

11. Pusey, William Allen: Roentgen Rays in the Treatment of Skin Diseases, J. A. M. A. **37**:820 (Sept. 28) 1901; Report of Cases Treated with Roentgen Rays, ibid. **38**:911 (April 12) 1902; A Subsequent Report on a Case of Carcinoma Discharged as Hopeless and Recorded as a Failure, ibid. **39**:487 (Aug. 30) 1902; The Rationale and the Indications for the Therapeutic Use of Roentgen Rays, J. Cutan. Dis. **29**:355 (Aug.) 1903; Therapeutic Use of X-Rays: Three Years After, J. A. M. A. **44**:1496 (May 13) 1905.

of radium for prolonged interstitial irradiation in selected cases of cutaneous malignant disease.

The object of all radiation therapy is to administer a lethal dose to each cell of the neoplasm. To obtain satisfactory clinical results it is necessary to administer a homogeneous dose sufficient to produce disintegration of the tumor with the least possible damage to the healthy surrounding tissues. We believe that this is best accomplished by means of the small platinum needle with multiple interstitial focal points of radiation.

DESCRIPTION OF NEEDLES

The platinum iridium needles used by us are of the French-British type and contain 1 and 2 mg. of radium element. Our needles contain slightly more radium element than the original needles described by Cade,[2a] which reduces the length of time the needles must remain in the tissue without altering the original purpose of prolonged irradiation.

Our small needles are 11 mm. long and 1.5 mm. in diameter, contain 1 mg. of radium element and have a wall thickness of 0.5 mm. of platinum. The larger needles are 27 mm. long and 1.85 mm. in diameter, contain 2 mg. of radium element and have a wall thickness of 0.6 mm. of platinum. This gives 1 mg. of radium element to each centimeter of active length of needle and when needles are implanted at 1 cm. distance gives proper distribution of homogeneous gamma rays to 1 cc. of tissue.

DOSAGE

It has previously been estimated that with needles of this type 100 milligram hours of irradiation per cubic centimeter of tissue will destroy squamous cell carcinoma without causing necrosis or sloughing. Therefore, our needles were at first allowed to remain in place for 100 hours, or four and one-sixth days. The time element has gradually been increased until at present they are allowed to remain in place for five or six full days, which gives from 120 to 140 milligram hours of irradiation. Recently one of us (B. S.) has prolonged the time to seven full days in the treatment of extensive clinically resistant lesions, producing 168 milligram hours for each needle. The erythema was only moderately increased and the epithelitis only slightly more marked; no evidence of sloughing or necrosis was observed. A dose this large has been used by Treves[7] and by Cole and Driver[8] in treating cutaneous malignant tumors with excellent results. The large dose apparently does not delay healing, which is usually complete in from three to eight weeks, depending on the size of the tumor treated. In marked contrast to the former method of interstitial irradiation with insufficiently filtered steel needles and subsequent necrosis due to beta

rays, the present method of prolonged irradiation with heavily filtered platinum needles is accompanied by little or no pain. Local pruritus is usually the most marked subjective symptom.

TECHNIC OF NEEDLE IMPLANTATION

The needles are implanted 1 cm. apart underneath and at the margins of the neoplasm, the usual surgical asepsis with local or block anesthesia being employed. We do not implant our needles directly into the tumor itself but always place them at the extending borders of the neoplasm, where irradiation is theoretically most needed. For the introduction of the needles a fine-pointed scalpel is used for making

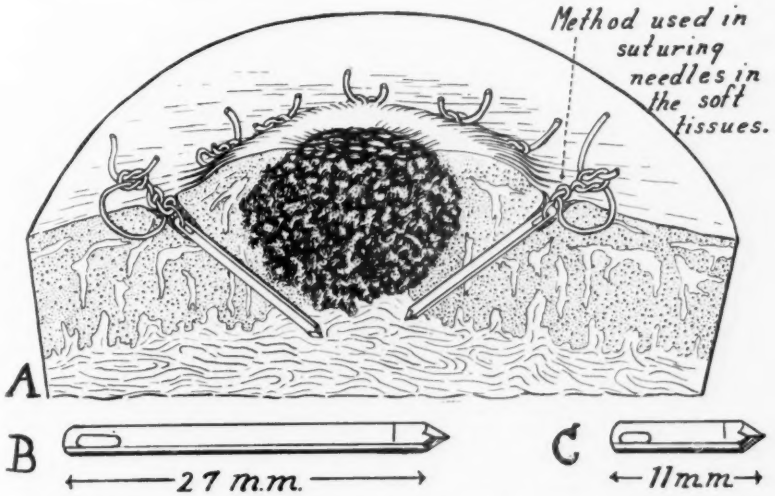

Fig. 1.—Schematic drawing showing types of needles employed and the method of implantation. *A*, surface and sagittal views of cutaneous malignant tumor with needles sutured in place, one needle to each cubic centimeter of tissue. The needles were allowed to remain in place for one hundred hours, producing 100 milligram hours per cubic centimeter. *B*, large needle, the dimensions of which are as follows: length, 27 mm.; diameter, 1.85 mm.; wall thickness, 0.6 mm. The wall is platinum; the needle contains 2 mg. of radium. *C*, small needle 11 mm. long and 1.5 mm. in diameter, having a wall thickness of 0.5 mm. and containing 1 mg. of radium.

a puncture wound, which facilitates the insertion of the needles. The eyelet of the needle is threaded with heavily waxed dental floss and tied so that there are a short, 2 inch, and a longer, 6 or 8 inch, suture. After the needles are inserted a small full-curved needle is threaded to the short suture, a transfixion suture is placed through the puncture wound and a tie is made with the two ends of dental floss suture. The longer, or guy, end is then attached to an adjacent area with adhesive tape. If one prefers, dermal suture may be threaded through the eyelet

of the radium needle and used for the transfixion suture, the dental floss being used only as a guy thread. In either case the needles are removed by clipping the transfixion suture and applying gentle traction to the dental floss.

INDICATIONS, ADVANTAGES AND RESULTS

The choice of cases of cutaneous malignant disease in which this method of implantation therapy should be used is governed by many factors. The method is especially valuable in treating extensive malignant lesions which are difficult to treat by any other technic, and it gives results superior to those obtained by any other method in the treatment of lesions which are situated adjacent to, or have produced infiltration of, bone or cartilage. Resistant lesions in any location, especially those which have failed to respond to other methods, and lesions with extensive formation of scar tissue are more amenable to this type of implantation therapy than to other methods. In general,

Fig. 2.—Pedunculated basosquamous cell carcinoma of the lower eyelid. The eyeball was not involved. Two needles containing 2 mg. of radium were implanted at the base of the growth for one hundred and twenty hours (five days). The total dose was 480 milligram hours. The second photograph was made one year later.

the technic is advantageous in cases of rapidly growing squamous cell carcinoma of any site, of extensive and infiltrative basal cell carcinoma and of a neoplasm overlying or involving bone or cartilage.

The primary advantages of implantation therapy over radium therapy externally applied are the homogeneous irradiation of the entire area of malignant degeneration and the continuous treatment over a prolonged period, with the resultant irradiation of the tumor cells during periods of mitotic division, when they are most radiosensitive. The prolonged continuous treatment prevents the development of radioresistance. The delayed time of healing which may follow the use of radon seeds or heavy doses of surface irradiation is avoided. The objectionable radiation inflammation of bone and cartilage is prevented, more accurate dosage is possible and the technic may be more safely applied to large areas without the danger of cutaneous sequelae such as result from surface irradiation. The greatest disadvantage is the necessity of hospitalization in many cases. When lesions of the skin

are irradiated with the needles well sutured and fixed dressings are applied, patients need not be hospitalized. In the treatment of malignant disease affecting movable areas, as the lip or the oral cavity, hospitalization is often required.

Fig. 3.—Large basal cell epithelioma infiltrating deeply into the tissues of the cheek. Six needles containing 2 mg. and three needles containing 1 mg. of radium were implanted underneath and at the margins of the growth for one hundred and twenty hours (five days). The total dose was 1,800 milligram hours. The second photograph was made one year later. There was no recurrence, and an excellent cosmetic result was obtained

Fig. 4.—Large, rapidly growing prickle cell carcinoma. Six needles containing 2 mg. of radium were implanted beneath and at the margins of the lesion for one hundred and forty-four hours (six days). The total dose was 1,728 milligram hours. The second photograph, made seven weeks after insertion of the needles, shows complete healing.

Fig. 5.—Prickle cell carcinoma of the index finger with attachment to underlying structures. Three needles containing 2 mg. of radium were implanted at the base of the growth for one hundred and twenty hours (five days). The total dose was 720 milligram hours. The second photograph was made eleven months later.

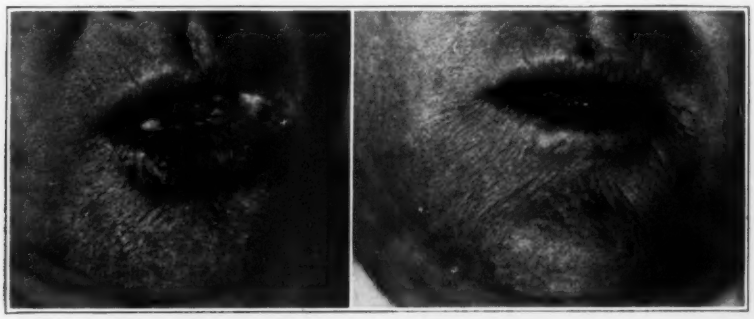

Fig. 6.—Prickle cell carcinoma infiltrating deeply into the subcutaneous tissues of the lip. Three needles containing 1 mg. of radium were implanted at the margins of the infiltrated area for one hundred and twenty hours (five days). The total dose was 360 milligram hours. The second photograph was made seven months later.

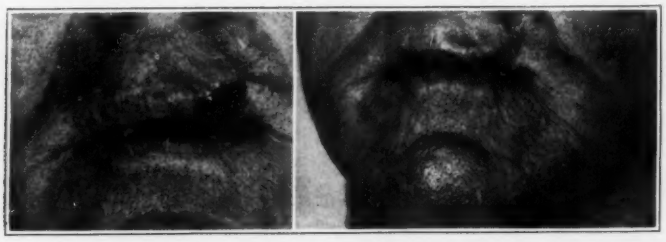

Fig. 7.—Recurrent prickle cell carcinoma in scar tissue at a site previously treated by a "cancer-paste." Two needles containing 2 mg. of radium were implanted at the margins of the growth for one hundred and twenty hours (five days). The total dose was 480 milligram hours. The second photograph was made one year later.

The results in our cases have been satisfactory, and cures have been attained which might not have been achieved by any other method. Recurrences following surgical treatment, desiccation or previous irradiation have responded rapidly. Our series of sixty-six neoplasms

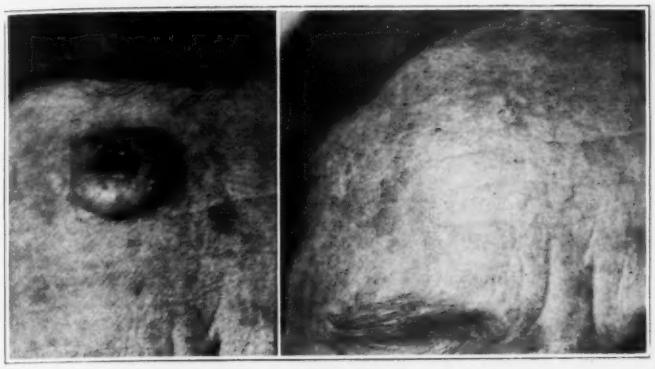

Fig. 8.—Prickle cell carcinoma of four months' duration. Three needles containing 2 mg. of radium were inserted at the base of the lesion for one hundred and nineteen hours. The total dose was 714 milligram hours. The second photograph was made three months later.

Fig. 9.—Prickle cell epithelioma of the nose. The lesion had received an unknown quantity (twelve treatments) of roentgen radiation one year previously. Nine needles containing 1 mg. of radium were implanted at the base of the growth for one hundred and ten hours. The total dose was 990 milligram hours. The second photograph was made four months later.

treated by this method includes lesions of the lip, nose, face, scalp, dorsum of the hand, side of the neck and other sites of skin and mucous membrane. Treatment in selected cases of intra-oral carcinoma by this technic has resulted in local cure, yet the percentage of metastatic lesions has apparently not been materially decreased.

SUMMARY

A method of radium implantation therapy in which the dose can be carefully and accurately measured is presented for use in treating cutaneous malignant disease.

Prolonged interstitial irradiation with heavily filtered platinum iridium needles of small radium intensity produces a homogeneous irradiation with selective gamma rays.

Photographs showing the lesion before and after treatment with a given dose of radiation are presented. Excellent cosmetic results are obtained, since protection is afforded the surrounding normal tissues because of the heavy filtration and the multiplicity of foci.

The method has been used by us for more than three years; it is continually becoming more useful, and its advantages are more readily recognized. It is recommended for use in selected cases of cutaneous malignant disease and not as a routine procedure for the treatment of surface and intra-oral neoplasms.

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ABSTRACT OF DISCUSSION

Dr. C. Ferd Lehmann, San Antonio: The application of this principle of radiation, i. e., application of heavily filtered rays in small doses over a continuous period, has two advantages: not only does it reach, and effect cures on, the so-called radioresistant cells but it also leaves a much healthier scar. I have noticed in the past few years that lesions so treated, particularly those on the lips, leave scars much more healthy than do lesions treated with monometal needles. This procedure has many advantages in treatment of epithelioma around cartilage in the nose and ear in cases in which reconstructive surgical measures will become necessary. However, this method of treatment is used in many cases of epithelioma in which other methods, such as curetting and electrodesiccation, could be employed. I think that eventually Dr. Shelmire's enthusiasm will wane and he will use the method only in carefully selected cases.

Dr. Harold N. Cole, Cleveland: My co-workers and I have used these radium platinum needles since shortly after Cade's text book (Radium Treatment of Cancer, New York, William Wood & Company, 1929) was published. Any dermatologist who is interested should read that book and review the type of treatment with gamma rays described in it. The method should not be used as a routine. I think that in many cases excellent results can be obtained with endothermy and curettage. On the other hand, there are many cases in which platinum needles containing radium are of great value. In cases of carcinoma of the lip certain types of lesions of the mucous membrane will respond better to this treatment than to any other.

The original treatment for carcinoma of the tongue was surgical intervention, and it is known that disastrous results followed that type of treatment. When radium began to be used it was first employed in the form of plaque application. Later the scheme was devised of using steel needles. This was not quite satisfactory. Still later Quick introduced the use of glass seeds. The reaction from glass seeds was tremendous, but several patients who were cured by the use of glass seeds exhibit extensive disfigurement. Then gold seeds were devised. The reaction from these was not so severe; nevertheless, it was considerable. Platinum radium needles and gamma rays provide the ideal treatment for carcinoma of the tongue. With the area under local anesthesia the needles are placed in position and sewed in, and string previously soaked in a 5 per cent solution of acriflavine hydrochloride to prevent digestion is attached to the individual needle and then brought outside the mouth and attached with adhesive tape to the cheek. It is remarkable how little discomfort these needles cause; within twenty-four hours after they are inserted the patient is able to eat tolerably well. When they are removed there is a reaction that appears in about ten days and lasts for from four to six weeks. The results are good in a fair proportion of cases, naturally not in all.

The needles are of great value in treatment of recurrence after radiation therapy. A patient may have received roentgen therapy, and the tumor may be bound down to the bone, making surgical treatment undesirable. In a case of that type platinum needles will produce surprisingly good results. One must be careful not to give too much radiation, for the tissue has lost much of its blood supply, and if too much radiation is used healing will be slow.

The scar left after this therapy is soft, supple and inconspicuous. The method is also of great value in treating lesions on the ear, which in the past have proved troublesome and in many cases have produced metastases. The same thing is true of lesions about the nose.

I think that dermatologists should use this method of therapy more often.

Dr. Howard Morrow, San Francisco: Nothwithstanding the fact that we treat epithelioma of the lip with electrodesiccation, my co-workers and I are still believers in radium therapy.

Dr. Cole referred to the treatment of lesions of the mucous membrane with radium, and I agree that it is the best method known. Dr. Taussig has long ago adopted the use of gold seeds, and the reaction which for many years followed the use of glass seeds does not result from treatment with gold seeds.

As to selection of cases, I am sure that eventually Dr. Shelmire will stop using radiation in treating carcinoma of the ear. One of these days he will have an experience which will make him believe in destruction of lesions of the ear by electrodesiccation and not by radium therapy.

It does not matter, as has been said, what type of treatment is used provided it is thorough. I think that fewer recurrences will follow desiccation than have followed radium therapy.

Dr. George Miller MacKee, New York: I wish to call attention to one point that has been a subject of controversy in the past but about which less is heard nowadays, namely, the danger of inserting anything in a malignant tumor—a knife, a punch, a radium needle or an implant. Years ago it was thought that this was a dangerous procedure because it led to metastasis. I have discussed this subject with almost every one of the well known cancer experts of the country and with many pathologists—Dr. Ewing, Dr. Francis Carter Wood, Dr. Douglas Quick and many others. I find now that the consensus is that there is no danger at all in

such a procedure. These experts say that there is danger if the lesion is squeezed unnecessarily or massaged but that the introduction of a sharp punch or needle is without danger.

The radium needle is a valuable method and should be, I think, used in selected cases. I think there are some cases in which it is better to use beta rays. I do not have time to go into details, but in cases of epithelioma of the eyelids, for example, I prefer to use needles or implants that will give intense beta rays. In that way there is much less danger to the eye.

I may have misunderstood Dr. Shelmire, but I thought he said that one could depend on obtaining cure in 95 per cent of unselected cases. That has not been my experience. I think that the highest incidence of cure that one can hope to obtain by any method in unselected cases is about 85 per cent. In selected cases of basal cell epithelioma of pure type and by the use of a selected method one can expect an incidence of cure of between 95 and 100 per cent on the basis of the five year period of observation. I believe that every dermatologist should be expert in all the accepted methods of diagnosing, determining radiosensitivity of tumors and grading and managing cutaneous malignant degeneration.

Dr. Laurence R. Taussig, San Francisco: The radiation therapy of malignant disease has been developing for thirty years and is still in flux. I think that ideas regarding radiation therapy change from year to year, partly because of what is learned about that form of therapy and partly on account of the development of other types of apparatus. The interstitial method was one of the earliest methods devised, and it has been greatly improved. At first radon contained in glass seeds was used, and I think that in some cases the glass seeds would give results superior to those obtained with gold seeds or with the new platinum needles. My co-workers and I still use irradiation in a number of cases of malignant degeneration. In some cases we use roentgen therapy. I think that some lesions, particularly those of the back of the hands, respond well to unfiltered roentgen radiation.

I do not agree with Dr. Shelmire that the implantation of seeds in involved lymph nodes is always hopeless. In a few instances my co-workers and I have implanted gold seeds in rather large lesions which the surgeon did not wish to remove, and within a few months the glands have become movable and fit for surgical removal. In a few instances long time cures have resulted.

Dr. Bedford Shelmire: We use this method of irradiation only in selected cases. Most of the epitheliomas seen in dermatologic practice can be treated effectively by Sherwell's method, electrothermic coagulation, cautery removal or even excision with the scalpel; all destructive methods should be followed by some form of irradiation. We employ all these methods in our practice.

We prefer these heavily filtered needles to gold seeds because of the lower expense, heavier filtration, ease of introduction and more homogeneous irradiation. After the initial purchase the needles are always available. After irradiation of the growth they are removed and are not left in the tissues as foreign bodies, as is the case with the seeds.

I agree with Dr. Morrow that most epitheliomas of the ear are readily curable by methods other than irradiation with these small needles. In certain selected cases these needles seem superior to any other form of treatment.

Dr. MacKee is certainly correct in advocating treatment with beta rays in most cases of epithelioma of the eyelids. As to the percentage of cures in cases of cancer of the skin, I still believe that I can effect a cure in more than 95 per cent of cases observed in private practice.

VITILIGO OF THE LIPS

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Vitiligo, except for the disfigurement it causes, is an uninteresting disease, as it is easily diagnosed, is an indication of no other known trouble and is in most instances absolutely refractory to treatment. It is manifested merely by an area of white skin surrounded by more deeply pigmented skin, as if the pigment had been shoved from this white center to the periphery. Formerly the condition was more interesting than it is at present, as it was thought to be a symptom of leprosy and the patient exhibiting it was expelled from his community, which was then equivalent to a death sentence; but that time has long passed.

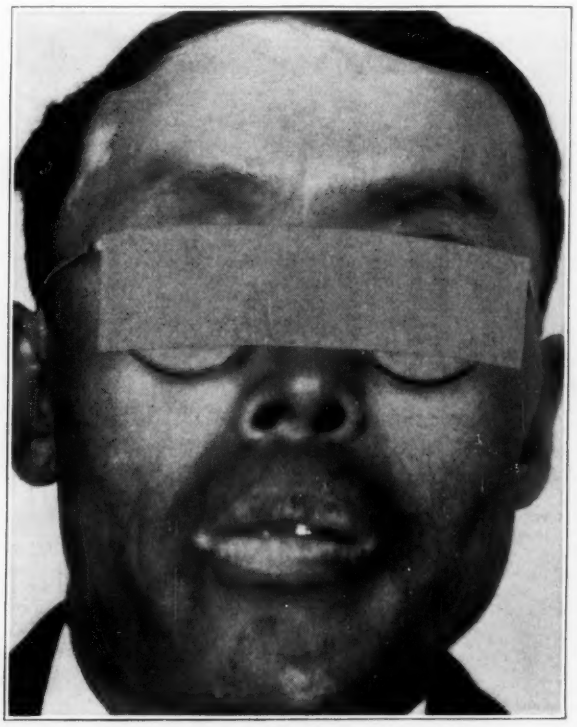
The statement that the area of vitiligo is white is not exact. It is white only by contrast. If a hole is cut in a piece of white paper and placed over the apparently white surface, thereby shutting out the surrounding, more deeply pigmented, skin, it will be found that the surface is not white but pink. This has a bearing on what is about to be related.

A Japanese farmer aged 39 consulted me in March 1936 because of scaly roughness of the lower lip. The upper lip was also affected but not nearly so extensively. There were numerous patches of vitiligo scattered over the body and limbs about which the patient was worried and for which he had received treatment by cauterization from a Japanese physician.

In examining the lips my interest was of course fixed on the superficial lesions, but I felt that there was something strange and unusual in the basic tint until it dawned on me that the lips as well as the skin were vitiliginous. Instead of being a deep red or even dark, as would be natural in a Japanese, the exposed portion was light salmon pink except in limited areas of the upper lip and also to a lesser extent of the lower lip, where it was deep brown. This was quite in accord with the picture of vitiligo in which the neighboring skin, as stated, always exhibits an excess of pigment.

The appearance may easily cause one to fall into error, as pigmented patches, especially on the exposed red portion of the lower lip, are not uncommon and, as Pusey long ago mentioned, are not necessarily serious. The pigmented areas exhibited by this patient, however, when once appreciated, appeared as something strange and unnatural, and the statement that the depigmented surfaces were salmon pink conveys lamely the impression they made.

Mention of such an occurrence as this is rare in the literature. Brünauer [1] and Coulon-Esquier stated that vitiligo of the mouth occurs only in Negroes, and Atkinson mentioned vitiligo of the labia minora and of the inner surface of the prepuce. In Pusey's textbook [2] there is an illustration showing vitiligo of the eyelids and of the lower lip in a dark-skinned person.



Photograph showing a characteristic white area over the right temple with the usual hyperpigmented skin about it, the more highly pigmented mucous membrane above the vitiliginous upper lip and the hyperpigmented area to the right on the lower lip. The latter is slightly blurred because of the scaling. The white areas at the corners of the mouth are characteristic and do not occur in leukoplakia.

The unusual situation was, however, not the only or even the chief interest in this case. It is repeatedly mentioned in the literature that

1. Brünauer, Stefan Robert: Atrophien, in Arzt, L., and Zieler, Karl: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935, p. 779.

2. Pusey, William Allen: The Principles and Practice of Dermatology, New York, D. Appleton & Co., 1917, p. 962. The illustration is from Heidingsfeld's collection.

the pigmented areas of vitiligo are unusually sensitive to actinic solar rays. The patient's home was near Stockton, Calif., which is at 37 : 50 degrees north latitude, the latitude of the southern part of Spain; he was therefore exposed to strong rays of the sun, though they were of about the same strength as those prevailing in his native country.[3] Confirmatory evidence of the effect of this irritation was shown by the fact that the lower lip was much rougher and more irritated than the upper. This continuous irritation in such a situation is a serious matter, as it leads to cancer.

As nothing could be done to repigment the lips and as the man's occupation was fixed, the therapy was naturally directed toward shielding the lips from actinic rays. Red is the best color for this. The principle of using a red shield is the same as that which is employed by photographers in changing photographic plates under a red light. This principle induced the farmer in the old days to use a red bandana to screen the back of his neck and the cowboy to use one to screen his face, with the difference that the farmer tied the knot in front and the cowboy tied the knot behind. In both instances the use of the bandana was a subconscious defense reaction. It may be possible for the cowboy to wear a red bandana over the face, but it is, however, impossible for a farmer to do so as the practice would interfere with his work.

The use of another kind of screen was suggested, one of the large umbrella-like hat so frequently seen in Japan, but never worn by Japanese in this country, probably because the Japanese, being highly sensitive, are averse to being made conspicuous by wearing such a hat.

Another screen is the common lip-stick, which is adherent and, if not perfumed, is usually nonirritating.[4] The patient therefore was advised to wear a broad-brimmed hat, to use a lip-stick during the day and to apply a mild adherent ointment at night.

By far the best screen, however, is the natural one provided by the moustache, and the dark color of the patient's moustache area, as seen in the photograph, was principally due not to the hyperpigmentation of vitiligo but to stout black hairs holding out a promise that if they were allowed to grow an excellent black screen would be formed. Why nature in the tropics and subtropics has chosen black, an absorbing color for radiant energy, as her favorite screening color for human beings while in the northwestern part of Europe, where the sun is weak, she has chosen red and yellow is one of her mysteries.

This was not my first experience with the moustache as an efficient screen. I had advised that natural protection in the treatment of solar

3. Tokyo, Japan, is a little north of 36 degrees latitude.

4. Baer, Harry Leonard: Lip-Stick Dermatitis, Arch. Dermat. & Syph. **32**:726 (Nov.) 1935.

irritability of the lower lip in 1911, in a case in which I became aware of the inefficiency as a screen for the lips of the red bandana for a man working on a farm.

Not much can be said in praise of the hairy covering of man. It is expensive to wear or to get rid of, and it harbors dirt, microbes and vermin and favors disease. As a coat it is ridiculously thin and ragged and has been superseded by clothing. It is cheering, however, to find, as in this case, that it has some use.

PROBABLE CASE OF THIRD GENERATION SYPHILIS

REPORT OF A CASE

CHARLES R. REIN, M.D.
AND
FRANCES SHOSTAC, M.D.
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Although third generation syphilis is exceedingly rare, there is sufficient evidence in the literature to show that it does occur. There are, however, a number of syphilologists of long experience who are skeptical of its occurrence. They have stated the belief that the majority of cases reported do not fulfil all the criteria first proposed by Fournier and Finger. Stokes,[1] who expressed the belief that most of the cases that have appeared in the literature were not beyond criticism, quoted these criteria as follows:

"(1) Acquired syphilis must be demonstrated in the grandmother and preferably also the grandfather. (2) Prenatal as distinguished from acquired syphilis must be demonstrated in the mother of the third generation case. Acquired syphilis must be excluded in her case and the father must be proved to be healthy. (3) There must be incontestable evidence of prenatal syphilis in the third generation; and (4) manifestations must appear soon after birth in both the second and third generation."

Rosenbaum and Faulkner[2] recently reported two complete family histories which they believe fulfil all the criteria for proving the occurrence of syphilis in the third generation. Smith and Howard, of Moore's clinic,[3] made a study of this condition and found that eighty-eight mothers with congenital syphilis had one hundred and seventy-one children, of which eight (4.5 per cent) had third generation syphilis.

The following complete case history is reported because we believe that it essentially fulfils the criteria proposed by Fournier and Finger:

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, Dr. George M. MacKee, Director, service of Dr. Fred Wise; and the New York Infirmary for Women and Children, Department of Obstetrics, Dr. W. A. Ragland, Director.

1. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934, p. 1270.

2. Rosenbaum, H. A., and Faulkner, H. L.: Third Generation Syphilis, J. Pediat. **7**:735, 1935.

3. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1934, p. 442.

REPORT OF CASE

The grandmother, aged 54, an Italian, first reported to her physician in 1920, complaining of nervousness. Her physician made a test of the blood and then gave her ten injections in the arm and the hip. She consulted one of us (F. S.) in November 1935, complaining of dizziness, noises in the right side of the head, diarrhea, restless sleeping, drowsiness, frequency of urination and nocturia. A test of the blood at this time was positive for syphilis. Her husband died at the age of 32, after an automobile accident. He had contracted a chancre many years previously and reported to his private physician for treatment. The physician did not remember the exact date on which the patient was first seen but thought that it was about twenty-four years previously. The patient received three injections but did not return for further treatment. From this union, which was not consanguineous, there were eight pregnancies. Six siblings were living and came under our observation. The status of each one as far as syphilis is concerned is given in chronological order according to the mother's pregnancy.

First Pregnancy.—Mrs. Fo. was born in 1907 and married Mr. Fo. in 1931; they had no clinical or serologic evidence of syphilis.

Second Pregnancy.—Mrs. Fi. was born in 1910 and married Mr. Fi. in 1930; they had no clinical or serologic evidence of syphilis. They had one child, who was born in 1931 and who was also free from evidence of syphilis.

Third Pregnancy.—C. C. was born in 1911, contracted whooping cough and died of convulsions at the age of 19 months. No evidence in the history suggested a syphilitic stigma.

Fourth Pregnancy.—Mrs. L. was born in 1912; at birth she presented no stigma of congenital syphilis as far as could be elicited from the history. Routine tests of the blood were made in 1935, when it was learned that her mother had syphilis. Mrs. L showed a 4 plus reaction to the Kline, Wassermann and Kahn tests of the blood. She married Mr. L. in 1931; he had numerous serologic tests, all of which gave negative results. They had one child, born in 1932, who presented no stigma of congenital syphilis. The Wassermann, Kline and Kahn tests of the blood, however, were strongly positive on numerous examinations. Mr. L.'s mother was also examined; she had no clinical or serologic evidence of syphilis.

Fifth Pregnancy.—The child, born in 1913, had a cold and snuffles from date of birth and "wasted away until she died, at the age of 4 months."

Sixth Pregnancy.—D. C. was born in 1915 and presented no stigma of congenital syphilis. The Wassermann, Kline and Kahn tests of the blood, however, elicited a strongly positive response on numerous examinations. He gave no history of having had a primary lesion or secondary eruption.

Seventh Pregnancy.—R. C., born in 1919, never presented any stigmas of congenital syphilis. Routine serologic tests performed in January 1936 gave the following results: Kline test, 2 plus; Kahn test, negative; Wassermann test, negative.

Eighth Pregnancy.—L. C. was born in 1921. He never presented any stigma of congenital syphilis, and the Wassermann, Kline and Kahn tests of the blood gave negative results on numerous examinations.

It is interesting that the mother had received intramuscular and intravenous injections immediately preceding and during the last pregnancy.

Roentgenograms of the long bones and of the skull of Mrs. L., her child and her brother (D. C.) disclosed no changes due to syphilis.

COMMENT

Acquired syphilis was demonstrated in both the maternal grandmother and the maternal grandfather. It is impossible, however, definitely to prove the occurrence of congenital syphilis in the mother of the patient with third generation syphilis, especially since she presented no stigma of congenital syphilis. Nevertheless, several facts strongly suggest this possibility:

1. The grandfather acquired his infection about twenty-four years previously, i. e., immediately before the birth of the mother of the patient with third generation syphilis.

2. The two older sisters were nonsyphilitic, while serologic tests of the younger brother were positive for syphilis.

3. The mother of the patient with third generation syphilis gave no history of having had a primary lesion or a secondary eruption during her early adult life. In addition, her husband had no clinical or serologic evidence of syphilis.

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LXXV.—MYCOLOGIC TECHNIC IN DERMATOLOGIC PRACTICE

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In every case of suspected mycosis the causative organism should be isolated and studied whenever practicable because from the academic standpoint the possibility of the presence of a new or different pathogen should not be overlooked.

The methods herein described are intended for use in routine office work.

SCRAPINGS, METHODS AND MATERIALS

The most common method used for the examination of scrapings is to mount the material in an alkali; either sodium hydroxide (NaOH) or potassium hydroxide (KOH) may be used. Potassium hydroxide is preferable; it should be used in a 10 to 30 per cent solution. For rapid work, a 40 per cent solution may be used, but it is not advocated. Too weak a solution takes a long time in clearing the skin, whereas too strong a one tends to swell and disintegrate the fungi. The length of time necessary for the clearing varies from five minutes to approximately two hours. A little heat often facilitates the procedure. It is not necessary to allow the material to stand overnight. Care should be taken when examining the slide (1) to ring it with paraffin to prevent evaporation and consequent crystallization and (2) to use subdued light in order to avoid high lights. The fungus appears distinct and is clearly discernible as contrasted with the irregular and nondescript appearance of the skin, which usually becomes clear.

The type of material to be examined varies with the several infections, and different methods of study should be applied to the scrapings. Of diagnostic importance, however, is the type of mycelium seen in the mounts, whether fragmented or continuous, simple or branched. The distribution of the spores and their size facilitate diagnosis.

In scraping lesions care should be taken to obtain portions from the active infection, particularly the border. In vesicular eruptions the

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From the Laboratory for Mycological and Dermatological Research of the Research Department of the Barnard Free Skin and Cancer Hospital.

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Drs. M. F. Engman and W. H. Mook.

fluid does not often contain the fungus except possibly in yeastlike infections. In eruptions caused by filamentous fungi the roofs of the vesicles should be examined and cultured. The lesion should always be cleansed with 70 per cent alcohol before the material is removed. This concentration is preferable to 95 per cent because of its greater ability to destroy the surface contaminants. In the case of ulcerated and crusted vesicular or papular lesions care should be taken that fresh infections are scraped to obtain active organisms.

The hydroxide method of examination is simple and often rapid, but unless it is used by one accustomed to its mode of action the results may be misleading. The observations may be confused with the presence in the mounts of structures which resemble fungi closely, such as crystals, the so-called "mosaic fungus" and distorted globules of fat. Consequently a number of methods using stains or dyes have replaced those using an alkali with marked success.

When the scales or scrapings are rather thick the stains are not used to great advantage, and recourse must often be had to potassium hydroxide. When the material is fairly thin, however, such as is the case in examination of dandruff scales for Pityrosporum ovale, of scrapings from pityriasis versicolor, of dermatomycoses of the ringworm type or even of pus, exudates and sputum, a 1 per cent aqueous solution of methylene blue and glycerin can be used as follow: One drop of the 1 per cent solution of methylene blue is placed on a clean slide, and the material is stirred within it. The scrapings should be thoroughly immersed in the stain. This is allowed to stand for approximately two minutes; then a clean cover slip is placed over the mixture and pressed down to flatten out the material and to express the excess solution. The superfluous stain is taken up by filter paper. A drop of glycerin is then placed along one edge of the cover slip and allowed to seep under, displacing the stain and giving a clear background to the stained material. The fungus appears bright blue.

Another method, which is similar, substitutes an undiluted Giemsa solution for the methylene blue. The Giemsa solution is made up with glycerin, and distilled water is placed along the edge of the cover slip in place of the glycerin used in the aforementioned method. This procedure has been followed with good results by Weidman. These preparations, however, are temporary, but they are of value in that they bring out detail and prevent shrinkage and distortion of the cells.

The value of cotton blue (aniline blue, China blue) and lactophenol mounts of tissue or material has never been strongly emphasized. It has been used almost exclusively for culture material and has been employed only occasionally for scrapings. The dye is made up as a 0.5 per cent aqueous solution. The lactophenol is made up as follows:

lactic acid (U. S. P.), 20 Gm.; phenol crystals, 20 Gm.; glycerin, 40 Gm., and distilled water, 20 Gm. A drop of the cotton blue is placed on the slide; the material is stirred up within it and allowed to stand for approximately two minutes. The cover slip is added and pressed down to squeeze out any excess dye, which is then taken up by filter paper. A drop of lactophenol is added to the edge of the cover slip and allowed to replace the cotton blue which dries out. The stain may be rapidly replaced by holding a bit of filter paper at the edge of the cover slip opposite the drop of lactophenol. This stain and the clearing agent (lactophenol) are useful in that the cell wall stains lightly as compared with the darkly colored central portion.

Swartz recently made the following modification in the lactophenol and cotton blue procedure: The scrapings are first placed in a 5 per cent solution of potassium hydroxide, heated somewhat and then washed in water. The material is then put into a drop of the combined cotton blue (0.5 per cent) and lactophenol. If the technic is successfully carried out, the fungi stain blue against a background which has been cleared by both the potassium hydroxide and the lactophenol. This procedure should be followed with care since the alkali (KOH) has a tendency to hinder the taking up of stain. The combined cotton blue and lactophenol tend to give a blue background and should therefore be used separately, as described.

A solution stronger than lactophenol for clearing is obtained by using the following ingredients: phenol crystals, 25 Gm.; lactic acid (U. S. P.), 25 Gm., and chloral hydrate crystals, 50 Gm. For thick material the following combination is recommended by Langeron: chloral hydrate crystals, 40 Gm.; phenol crystals, 40 Gm.; lactic acid (U. S. P.), 20 Gm., and sodium salicylate, 10 Gm. A little heat facilitates clearing.

The investigation of infections of the scalp and hairy regions of the body often necessitates the examination of hairs. The standard method is to mount the hair in a 30 or even a 40 per cent solution of potassium hydroxide and let the mount stand for a few minutes. The application of a little heat hastens the clearing. It is advisable to dip the hairs taken from scalps, particularly those that are oily, in ether or in alcohol (absolute alcohol is preferable to 95 per cent alcohol) for a moment in order to get rid of the oil, which often simulates spores in shape and size.

Occasionally one has to examine a specimen for blastomycosis or torulosis. The presence of a double-contoured cell wall is of chief diagnostic interest, particularly in torulosis. In blastomycosis the wall is thick; the cell may be spherical, ovoid or budding and may be seen in a water mount. The organism of torulosis, Cryptococcus histolyticus, is

surrounded by a thick mucoid capsule and, unless distinguished by this characteristic, may be confused with the organism of blastomycosis. The method advocated by Weidman is the wet india ink technic: The suspected material is stirred in a drop of india ink, placed on a clean slide and covered with a cover slip. Care must be taken to work rapidly before the ink dries out. A small drop should be used so as to form a thin film. Against a dark background the capsule shows up as a clear halo surrounding the fungus. Spinal fluid may also be examined by this technic, although the background will not be as dark, owing to the dilution of the ink. Stains are not necessary for the organism, and they tend to spoil the effect of the ink.

These are but a few of the many technics in use. No doubt some prove more satisfactory than others to different dermatologists. A number of procedures not mentioned here may find greater favor with various technicians, but they require greater care, greater technical ability and a longer time for completion.

ISOLATION AND CULTIVATION OF THE PATHOGENS

When it has been proved by scraping or fluid mounts that a fungous infection is present, a culture should always be made. A number of mediums may be used; most of them, however, do not completely satisfy the requirements for the cultivation of a fungus. Nutrient mediums with a hydrogen ion concentration around the neutral point are generally to be avoided for isolation work, since the fungus grows comparatively slowly, if at all, and the nutrients form a good base for the growth of contaminating bacteria. This may be remedied in some mediums by the addition of a little lactic acid (85 per cent dilution of lactic acid U. S. P.) to the sterilized medium before it has cooled. The acid hinders the growth of bacteria. If infection with filamentous fungi is suspected, a clear or light medium should be used because the pigment which is liberated by some fungi and diffuses through the medium is important in determining the classification of the organism. It is advisable to cleanse the lesion with 70 per cent alcohol to help rid it of contaminating bacteria. Strenuous methods should be avoided, for if they are employed the fungus on the surface may also be killed and the scrapings or scales may become useless for culturing. The material is then obtained and inoculated in the medium.

The most widely used and general medium for fungi is a modification of Sabouraud's original formula. This is prepared from 10 Gm. of peptone, 40 Gm. of dextrose, 15 Gm. of agar, and 1,000 cc. of tap or distilled water. The ingredients are dissolved by boiling for a few minutes while being stirred, dispensed in test tubes or other containers and sterilized at 120 pounds' (54.4 Kg.) pressure for twenty minutes;

the medium is then allowed to cool and if put in test tubes is slanted. The final medium has a p_H of about from 5.2 to 5.6. Maltose may be used in place of dextrose, but the latter is preferable for trichophytoses in general. It is a clear substrate and allows for the distinguishing of diffused pigments. The original Sabouraud proof agar is made up with raw Chanut dextrose and granulated Chassaing peptone. These materials are difficult to obtain and are not always reliable as to purity or composition. It is therefore much better to adhere to a formula of definitely known constituents, such as the modification mentioned here. In addition to being clear the medium brings out markedly a number of cultural characteristics.

When the fungus has been grown on Sabouraud's modified maltose or dextrose agar and then studied, it is advisable, if the organism is to be maintained for purposes of teaching or of comparison, to grow it on a substrate that will not alter its morphology to any great extent or cause a loss of such anatomic features as spirals, fuseaux, characteristic spore formation and cultural appearance. A medium known as conservation agar is used. This, too, is a modification of Sabouraud's original constituents and is composed of the following ingredients: peptone, 30 Gm.; agar, 15 Gm., and tap or distilled water, 1,000 cc. The principle involved centers around the lack of carbohydrate, the presence of which has an effect in changing morphology.

For the isolation of yeast Sabouraud's maltose agar has been used rather successfully. The best known medium, however, is wort agar, prepared by the following formula (Difco): maltose, technical, 12.75 Gm.; malt extract, 15 Gm.; dextrin, 2.75 Gm.; glycerin, 2.35 Gm.; di-potassium phosphate, 1 Gm.; ammonium chloride, 1 Gm.; peptone, 0.78 Gm. and agar, 15 Gm. When sterilized, the medium has a final p_H of approximately 4.7. A modified wort agar, malt extract agar (Difco), is not as efficacious as the wort agar.

One of the chief factors in the value of wort agar, in addition to its being a good substrate for yeasts, is its ability to eliminate almost entirely the growth of contaminating bacteria. This is due to its high hydrogen ion concentration which has no effect on yeasts but is harmful to bacteria.

There are a number of other mediums which may be used, some for isolation purposes and others for subculturing and propagating the fungus. These, however, should be left for the mycologist in his further work on the microbe.

STUDY OF THE FUNGUS AND ITS LIFE CYCLE

The important characteristics to be noted in the life cycle of a fungus are the development of the mycelium, the formation of the blastospores,

arthrospores and so-called oidiospores, the evolution and production of asci and ascospores, if present, and that of other mycelial structures, such as conidia, conidiospores, chlamydospores, hypnospores, sporangia and sporangiospores, penicilli, spirals, aleuriospores, fuseaux and racquet mycelium and several others.

There are two main types of substrates to be used in carrying out these studies, the wet and the solid preparations. When the wet preparations are used the technic consists of the inoculation of a small amount of a liquid medium in such a way that the whole can be observed with a microscope. There are several ways of making these mounts, but those most commonly used are the van Tiegheum cell, the concave slide and the Ranvier cell. The van Tiegheum cell is probably the most commonly used. It consists of a collar of glass from 1.5 to 2 cm. in diameter and from 0.5 to 1 cm. in length, which is made to adhere to a glass slide either with Canada balsam (the oleoresin of fir) or some other adhesive. This forms a chamber, at the bottom of which it is advisable to place a drop of the medium to be used. A small drop of the liquid is also placed in the center of a cover slip large enough to cover the exposed edge of the glass collar which has been covered with sterile petrolatum or hydrous wool fat. The drop is then inoculated with the fungus, and the cover slip is inverted rapidly and placed on the glass collar. The cover slip is pressed down firmly so that it adheres tightly, with the petrolatum or hydrous wool fat acting as the adhesive. There is formed a relatively air-tight chamber from which the liquid medium will not evaporate readily.

In place of the van Tiegheum cell, the depressed, concave slide may be used in much the same manner.

The third type of cell consists of a glass slide with a flattened oval depression. A deep groove surrounds the cavity. This is known as the cell of Ranvier. It is sealed in the same manner as the aforementioned slides. Its chief attributes are that when the depression is filled with the liquid medium, inoculated and covered, there is an extremely fine space between the cover slip and the slide; it is filled with liquid and is therefore much larger than a hanging drop; the germinating spore or fruiting body can be watched with ease. It surpasses the hanging drop further in that it does not require a great deal of focusing. In all these preparations all the materials should be sterile, and the manipulator should work rapidly to avoid contamination.

The liquid medium to be employed may be one of the usual broth substrates, such as nutrient broth, liquid wort (wort medium minus the agar), Sabouraud's medium minus the agar, 2 per cent peptone (bactopeptone, proteose or Witte's peptone), 2 per cent peptone plus 2 per cent dextrose or any special medium that may be desired. A

little glycerin may be added to a hanging drop medium. This is an added nutrient which keeps the broth from evaporating rapidly.

In place of the liquid a solid substance may be used. The medium is dissolved and a drop placed on a cover slip—in much the same manner as is the liquid drop—and inoculated before it has completely cooled. On the other hand, a small amount of the dissolved medium may be inoculated when it has cooled sufficiently not to kill the fungus and placed on the cover slip. A clear nutrient agar is always advisable. A clear nutrient or peptone medium with gelatin as a solidifier gives a transparent substrate. A better preparation, in place of the hanging drop culture, is made as follows: A drop of dissolved gelatinized medium is placed on a clean sterile slide, inoculated and covered with a sterile cover slip, which is pressed down firmly to allow only a thin space of gelatin between the cover slip and the slide, and the preparation is ringed with sterile petrolatum or hydrous wool fat or, preferably, paraffin.

It is often desirable to trace the change of a fungus from the parasitic to the saprophytic mode of life or to determine some phase of its cycle which is usually lost after subculturing. This can best be accomplished by mounting some of the scrapings, pus, sputum, spinal fluid or other material directly in medium, liquid or solid, by one of the aforementioned methods and then observing its evolution. This is particularly recommended for the yeasts and yeastlike organisms.

The further identification of a fungus, particularly a yeast, involves further biochemical reactions, such as liquefaction of gelatin, fermentation of carbohydrates, acidification and curdling of milk, and special features, such as spore production. Single spore cultures are also often necessary, but this involves special technic and the use of expensive apparatus and should therefore be left to one accustomed to this type of work. The materials and technics presented here, though not new and for the most part not original, should be sufficient for examination of the usual mycoses encountered by the dermatologist in his office.

Minor Notes

SUCCESSFUL TREATMENT OF RAYNAUD'S DISEASE WITH ESTROGENIC SUBSTANCE

EDMUND W. KLINEFELTER, M.D. YORK, PA.

On Oct. 30, 1935, a 34 year old, well developed and healthy-appearing woman, 5 feet, 3 inches (1.6 meter) tall and weighing 136 pounds (61.7 Kg.), consulted me because of paroxysmal attacks of blueness, pain and numbness in her fingers. The history and physical examination disclosed that the patient had suffered from Raynaud's disease for the past seven years. During that time the attacks had progressed in severity; they disturbed the patient most at the time of menstruation, and she was comparatively free from discomfort during the intermenstrual interval. Usually a series of hot and cold flashes resembling menopausal hot flashes preceded an attack. The menstrual history was otherwise irrelevant except for the fact that a gradual diminution in the duration and amount of the flow had occurred in the past seven years. Laboratory studies revealed nothing of significance. The urine contained no albumin, sugar or hemoglobin. The Wassermann reaction of the blood was negative.

Examination during an attack showed that the hands became cold, blue and covered with sweat. The feet were only slightly involved. Pulsations were of good volume in both radial arteries.

The patient had received a wide variety of treatments, including administration of various tonics, and ammonium chloride, application of stimulating ointments and liniments, a ketogenic diet, contrast baths, Bier's hyperemia, galvanism, regular massage, dry heat and short wave diathermy. One physician advised injection into the sympathetic nerves or ganglionectomy.

For two months I prescribed large doses of calcium gluconate and ammonium chloride orally, but there was no improvement. Antipyrine, acetophenetidin and codeine, however, relieved the pain.

Since the paroxysms were associated with a menstrual disturbance and since the estrogenic substance not infrequently alleviates the hot and cold flashes of the menopause, 4,500 international units of estrogenic substance in oil was given intramuscularly on alternate days for seven doses. The medication was discontinued ten days before the onset of the menstrual period. A distinct improvement followed. The heat flashes and attacks of cyanosis in the fingers became markedly less severe. The periods lasted longer, and the flow became more free. After a repetition of the same treatment for two consecutive months the periods returned to normal, and all evidences of Raynaud's disease vanished. Since that time the patient has received no treatment. The periods have remained normal, and there have been no associated heat flashes or disturbances in the extremities.

COMMENT

Numerous reports appear in the literature indicating that in some cases a beneficial influence is derived from administration of estrogenic substance in the treatment of certain cutaneous diseases, but little reference is made to the use of this substance in the management of cutaneous diseases in which there is a conspicuous vasomotor component. Recently Drips and Brunsting[1] noted benefit from the administration of estrogenic substance in the treatment of urticaria, and

Janson [2] reported excellent results from its use in a case of severe axillary hyperhidrosis. A search of the literature, however, disclosed no report of a disorder such as that which I have described in which benefit followed the use of estrogenic substance.

546 West Market Street.

1. Drips, D. G., and Brunsting, L. A.: Urticaria and Endocrine Dysfunction, Proc. Staff Meet., Mayo Clin. **10**:764 (Nov. 27) 1935.

2. Janson: Schwere Hyperhidrosis axillaris und deren Heilung durch Progynon, Med. Klin. **32**:121 (Jan. 24) 1936.

TREATMENT OF PAINFUL SITES OF INJECTIONS

LESTER HOLLANDER, M.D., AND JOSEPH M. SHELTON, M.D., PITTSBURGH

In a few cases ultrashort wave therapy was used for the alleviation of pain following intramuscular injections or the use of sclerosing agents for various ulcers. The result was so satisfactory that this brief communication is made in the hope that others may avail themselves of this form of therapy. The apparatus used was a 6 meter ultrashort wave appliance with glass electrodes; the length of exposure was ten minutes, and treatments were repeated every second day.

Four patients with pain at sites of injections of a bismuth preparation received two treatments each according to this method, complete disappearance of pain resulting in the four instances; two patients with severe pain from injections into varicose veins received five treatments each, complete relief from pain resulting. In one patient with pain due to injection of histidine hydrochloride who received only one treatment satisfactory results likewise occurred.

631 Jenkins Building.

From the Pittsburgh Skin and Cancer Foundation.

TREATMENT OF ERYTHEMA INDURATA (BAZIN'S DISEASE)

ANDREW L. GLAZE, M.D., BIRMINGHAM, ALA.

The treatment of erythema indurata (Bazin's disease) is not quite satisfactory.

In a young woman with the nonulcerative form of this disorder, which proved unresponsive to the usual constitutional remedies and measures, apparent complete relief with rapid resolution of the infiltrations in the hypoderma followed daily application for three weeks of a mixture of equal parts of collodion U. S. P. and flexible collodion U. S. P. The affected areas and the sound skin for some distance around were painted with the mixture. Each new application was made over the previous ones. The almost startlingly favorable result appeared to have come about as a result of local splinting of the parts from the continuous contractile action exercised by the topical agent.

News and Comment

PROGRAM NOTICE, ATLANTIC CITY MEETING OF AMERICAN MEDICAL ASSOCIATION

Applicants for a place on the program of the Section on Dermatology and Syphilology of the American Medical Association at the meeting in Atlantic City, N. J., from June 7 to 11, 1937, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of the section, Dr. Bedford Shelmire, Medical Arts Building, Dallas, Texas.

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests.

Correspondence

USE OF TRYPARSAMIDE IN PRIMARY STAGES OF SYPHILIS

To the Editor.—I wish to correct a seemingly serious ambiguity in my recently published paper on tryparsamide (ARCH. DERMAT. & SYPH. **34**:582 [Oct.] 1936). It appears that certain of my colleagues are laboring under the impression that I am advocating the use of tryparsamide alone in the primary stages of syphilis. This interpretation is as incorrect as it is difficult to understand, for in the summary of the aforementioned article I stated that tryparsamide has but a mediocre effect in suppressing early lesions. Indeed, the small amount of work done with the drug in cases of primary syphilis (two cases) indicates only too well that at the time the report was made the work was in the nature of an experiment which was undertaken with no small degree of trepidation. I merely advocated that tryparsamide be incorporated into the curriculum of the Cooperative Clinical Group as outlined for early antisyphilitic therapy in the hope that tryparsamide might have some effect in reducing the ultimate incidence of neurosyphilis. My plan was to use tryparsamide on alternate weeks during the phase of treatment with heavy metals.

H. SUTHERLAND-CAMPBELL, M.D.
1930 Wilshire Boulevard,
Los Angeles.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

COMPARATIVE CHEMOTHERAPEUTIC STUDIES OF "ARSENOXIDE" (3 AMINO-4-HYDROXY-PHENYL-ARSENOXIDE) AND NEOARSPHENAMINE. G. W. RAIZISS and M. SEVERAC, Am. J. Syph. & Neurol. **19**:473 (Oct.) 1935.

Recently the attention of syphilologists has been called again to arsenoxide as an antisyphilitic agent. The authors made an experimental study of the toxicity and therapeutic efficiency of arsenoxide as compared with that of neoarsphenamine. As a result of their investigations they conclude that neoarsphenamine is far superior to arsenoxide in both trypanocidal and spirocheticidal properties. In rabbits with experimental syphilis the maximum tolerated dose and the minimum curative dose of arsenoxide are practically identical; this suggests that the clinical use of this drug in adequate curative doses may be fraught with considerable danger.

A PRELIMINARY STUDY OF THIO-ARSENE, DISODIUM BIS-(P-SULFOPHENYL) (ACETAMIDOPHENYL)-DITHIO-ARSENITE. C. R. ECKLER and H. A. SHONLE, Am. J. Syph. & Neurol. **19**:495 (Oct.) 1935.

Over twenty compounds comprising combinations of over eight arsenoxides with five thio-acids were studied. The substance finally selected for clinical study was di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite. It is a definite chemical substance containing 11.88 per cent arsenic. When dry, it is stable in air. In the absence of air aqueous solutions have been kept without deteriorating for one and a half years. Oxidized solutions have proved to be less toxic than the original solutions. The toxicity of this drug is lowered by the addition of sodium para-thiophenyl sulfonate, and there does not appear to be any loss of trypanocidal effectiveness when both are given.

In clinical and experimental work a stable solution in ampules has been used, each cubic centimeter containing 0.025 Gm. of di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite and thiophenyl sulfonic acid to the extent of from 2.25 to 2.75 times the weight of the former. Sufficient mono-ethanolamine is then added to give the solution a p_H between 8 and 9.2.

Trypanocidally di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite is twice as potent as arsphenamine, weight for weight. The drug is excreted largely by the kidneys and intestines. In human beings most of the arsenic given may be recovered by the end of five days. The average spirocheticidal potency of the drug in ampules is 20.6 mg. per kilogram, while the potency of arsphenamine is 15 mg. per kilogram. However, on the arsenic basis the arsenic in the former is at least twice as potent as the arsenic in the latter.

CLINICAL OBSERVATIONS ON THE TREATMENT OF SYPHILIS BY A COMBINATION OF BISMUTH SALICYLATE AND A NEW ARSENICAL SYNTHETIC. S. W. BECKER and M. E. OBERMAYER, Am. J. Syph. & Neurol. **19**:505 (Oct.) 1935.

This report concerns a clinical study of a new arsenical synthetic drug, di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite, used in combination with bismuth subsalicylate in the therapy of syphilis. About 4,000 injections have been given 291 syphilitic patients during the past three years.

The drug when administered with bismuth subsalicylate acts less rapidly, clinically and serologically, than arsphenamine used in the same way, but late relapses following combined treatment did not occur in Becker and Obermayer's series of 291 patients. Reactions consisting of nausea, vomiting and diarrhea occurred after from 20 to 30 per cent of the total number of injections given.

Retarding the rate of injection reduced the reactions by more than 50 per cent. Jaundice developed in 8 of 291 patients; all recovered. Dermatitis and hemorrhagic accidents were not encountered.

Becker and Obermayer believe that their experience entitles the drug in combination with bismuth subsalicylate to serious consideration in syphilotherapy.

THE THERAPEUTIC VALUE OF THIO-ARSENE: A CLINICAL STUDY OF THE THERAPEUTIC EFFICIENCY AND TOXICITY OF DISODIUM BIS-(P-SULFOPHENYL) (ACETAMIDOPHENYL)-DITHIO-ARSENITE, BASED ON 2,282 INJECTIONS ADMINISTERED TO 251 PATIENTS WITH SYPHILIS. W. H. CONNOR, H. C. SHAW, E. A. LEVIN and R. B. PALMER, Am. J. Syph. & Neurol. **19**:514 (Oct.) 1935.

The authors found that di-sodium bis (para-sulfophenyl) (acetamidophenyl)-dithio-arsenite does not possess a high degree of therapeutic efficiency even when administered biweekly in the highest tolerated doses. From their clinical study they conclude that the drug is probably not suitable for the treatment of syphilis, especially since more efficient and better tolerated preparations are available.

THE TREATMENT OF SYPHILIS WITH A NEW ARSENICAL DRUG. H. M. ROBINSON and J. E. MOORE, Am. J. Syph. & Neurol. **19**:525 (Oct.) 1935.

This paper presents the results of another clinical study of the new arsenical compound di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite in the treatment of early stages of syphilis. The drug was employed alone, no other form of antisyphilitic treatment being given.

This preparation produced gastro-intestinal reactions in such a large proportion of cases even when the advised dose was reduced that many patients were unwilling to submit to continued treatment with it. The drug is not utilizable in treatment of patients who have previously been sensitized to the arsphenamines. It provoked a fresh dermatitis in seven of eleven patients thus sensitized.

As to therapeutic efficacy the preparation compares unfavorably with any of the arsphenamines or with bismuth preparations in its effect on the disappearance of surface organisms in open lesions, on the healing of lesions and on the Wassermann reaction of the blood.

Robinson and Moore conclude that the drug in its present form is not entitled to serious consideration in syphilotherapy.

REUTER, Milwaukee.

HEREDITARY ECTODERMAL DYSPLASIA OF THE "ANHYDROTIC TYPE." S. J. THANNHAUSER, J. A. M. A. **106**:908 (March 14) 1936.

The symptomatic triad of this malady consists of complete inability to sweat, a deficiency of scalp, axillary and pubic hair, and incomplete development of the teeth. Other findings in most instances include saddle nose, a decrease in the intellect and a deformity of the auricles. In some cases only the hair and nails are affected. Usually a definite hereditary factor is present, the transmission being recessive and obligatory to the male sex. In the case reported by Thannhauser the patient had a pedigree confirming the fact that the transmission was recessive and obligatory to sex. He did not perspire until his sixteenth year. There were signs of insufficiency of the adrenal medulla, and the roentgenograms of the skull showed bony deformity.

HISTORY TAKING IN ALLERGIC DISEASES. FRANCIS M. RACKEMANN, J. A. M. A. **106**:976 (March 21) 1936.

In allergic diseases, the history is the chief diagnostic measure. Rackemann advises that a careful history should include all the ordinary questions usually related to a diseased state. Particularly important, however, in obtaining a history of a patient with eczema or other allergic disease, are (1) the family history and (2) the particular history of the complaint. The latter should include exact dates and not casual time periods. It is necessary to account for all the

time, both during an attack and during periods in which the patient is free from the disturbance. It is also important to trace the effect of change of residence, occupation, habits, diets, etc. Elimination of suspected allergens, both in the diet and in the surroundings, may be an important diagnostic procedure. Rackemann states that dusts as well as foods may cause atopic eczema.

ARGYRIA BECOMING MANIFEST IN PREGNANCY. JOHN RAAF and H. K. GRAY, J. A. M. A. **106**:916 (March 14) 1936.

Raaf and Gray report the case of a woman who fifteen years before underwent a tonsillectomy and during the next five years used a throat spray containing mild protein silver twice a day. Near the end of that five year period she gradually discontinued the practice, and for six months before the beginning of a pregnancy (nine and a half years before she was seen by Raaf and Gray) she had not used the spray. In the first month of the pregnancy a discoloration appeared and gradually spread over the entire body, and it has remained unchanged since that time. The clinical diagnosis was confirmed by the finding of silver granules in the gallbladder and appendix, which were removed at operation. The deposition of silver in the skin is thought to have been due to a disturbance in metabolism attributable to pregnancy.

THE ANTERIOR PITUITARY-LIKE HORMONE: A CLINICAL STUDY OF ITS EFFECTS IN ACNE VULGARIS. CHARLES H. LAWRENCE, J. A. M. A. **106**:983 (March 21) 1936.

Although further study is necessary to determine the exact nature of the endocrine imbalance, investigations point to a dysfunction in either the gonads, the pituitary gland or both as a cause of acne vulgaris. Thirty patients with acne were treated by means of injections of 2 cc. of the gonadotropic hormone of the urine of pregnant women (antuitrin-S) every other day. Ten patients were regarded as cured, and eleven others were much improved.

TULAREMIA. HAROLD L. AMOSS and DOUGLAS H. SPRUNT, J. A. M. A. **106**: 1078 (March 28) 1936.

Amoss and Sprunt report on two patients with tularemia in whom infection developed after ingestion of a rabbit. It was assumed that the rabbit was not well cooked. In the first patient the onset of the disease occurred about eight hours after he had eaten part of the rabbit. The disease was ushered in with pain in the left side of the chest and a severe chill; later gastro-intestinal symptoms and high fever ensued. Shortly thereafter the patient became stuporous and irrational. The course of the disease was steadily downward until death, which occurred thirteen days after the onset. Agglutination for Bacterium tularense was positive in a 1:640 dilution of serum. The anatomic diagnosis was tularemia; there were focal necrosis in lymph nodes and in the spleen and lungs, focal accumulation of round cells in the liver, interstitial monocytic pneumonia, lobular pneumonia and pulmonary emphysema. In the second patient, who ate part of the same rabbit as the first patient, a similar series of events and a fatal outcome also occurred. In this patient, however, repeated agglutination tests of the blood for Bacterium tularense gave negative results. Only three other cases have been reported in which tularemia developed from the ingestion of diseased rabbits.

THE SUBCUTANEOUS INJECTION OF ALCOHOL FOR PRURITUS ANI. BENJAMIN HASKELL and CLARENCE D. SMITH, J. A. M. A. **106**:1248 (April 11) 1936.

Haskell and Smith advocate the subcutaneous injection of alcohol for the relief of pruritus ani. They found that in a series of twenty-two patients, observed for a year or more, sixteen obtained complete relief, four remained com-

fortable, and two failed to obtain relief. Only small segments of perianal tissue were treated at one time. A 2 per cent solution of procaine hydrochloride was used to prevent pain during and after the injection. From 3 to 5 cc. of a 70 per cent solution of ethyl alcohol was injected at one time, care being taken not to harm any of the deeper tissues. From two to six such injections were required. The only complication encountered was slight sloughing, which occurred in six of the twenty-two patients.

LEWIS, New York.

CONTROL OF PIGMENT MIGRATION WITHIN THE CHROMATOPHORES OF PALAEMONETES VULGARIS. F. A. BROWN JR., J. Exper. Zoöl. **71**:1 (July 5) 1935.

All the movements of the pigments within the chromatophores of the shrimp, Palaemonetes vulgaris, are controlled by hormones, and each pigment is controlled by an independent hormone. Concentration of the white pigment is produced by a hormone formed in the eyestalks and in some tissue of the anterior region of the cephalothorax. Concentration of the red and the yellow pigments is produced by hormones formed in the eyestalks and in the central nerve organs. There is some evidence that a hormone is contained in the eyestalks which controls the blue pigment. Dispersion of the pigments may be explained by the absence of the pigment-concentrating hormones. The eyes are the only receptors involved in the responses of the chromatophore system of Palaemonetes.

WYMAN, BOSTON. [ARCH. NEUROL. & PSYCHIAT.]

SYPHILIS AND MENTAL DISEASES. WILLIS E. MERRIMAN, J. Social Hyg. **21**:164 (April) 1935.

During the year ending June 1933, syphilis was considered a causative factor in the cases of 11.3 per cent of all new patients admitted to the civil state hospitals. In 1931 Pollock computed the annual economic loss resulting from mental disease due to syphilis in the state of New York as approximately $13,500,000. The incidence of dementia paralytica in that state is nearly three times as great in cities as in rural districts when the estimate is based on respective urban and rural populations. Of over 16,000 patients with dementia paralytica admitted to the state hospitals during two recent decades, 13,000 died within an average of less than two years after admission. Modern methods of treatment have proved to have a decided advantage over earlier ones, but apparent recoveries are secured only in a distinct minority of cases.

FERGUSON, Niagara, Falls, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

HEREDITARY ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE WITH REPORT OF TWO CASES. EDWIN G. SCHWARZ, South. M. J. **28**:606 (July) 1935.

The authors report two cases of hereditary ectodermal dysplasia of the anhidrotic type. This rare condition is apparently always hereditary. The defects are developmental anomalies involving structures of ectodermal origin, and patients with this disorder are unable to perspire. The skin, together with the sweat glands and sebaceous glands, the nails, hair and teeth, the external organs of special sense, the nervous system and the mucous membranes of the mouth, nose and anus, are involved.

One of the children was 8 years old and the other 6.

The etiology is undetermined. Although children with this disease commonly show pronounced saddle nose, syphilis is usually not an etiologic factor. The same is true of tuberculosis. No positive endocrinopathy has been found, although many patients have been given thyroid extract because of the condition of the hair, nails and skin. There seems to be no effective treatment for the condition.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

BIOLOGICAL THERAPY IN VIRUS DISEASES. R. T. BRAIN, Brit. J. Dermat. **48**:21 (Jan.) 1936.

Brain reports five cases of recurrent herpes treated successfully with specific vaccine. In general, the interaction of virus and specific antibody can be demonstrated by such reactions as complement fixation, agglutination, precipitation and neutralization. In the work on complement fixation a 10 per cent suspension of herpetic pads from guinea-pigs proved to be a satisfactory antigen, and such a suspension inactivated with an 0.08 per cent solution of formaldehyde in saline solution was used for specific vaccine therapy. Brain briefly considers the subject of immunity in diseases caused by a virus and the rationale of biologic therapy. He suggests that the failure to cure molluscum contagiosum and warts by vaccines may be due to the fact that the intracellular virus is protected from circulating antibodies by the selective nature of the cell membrane.

A CASE OF DERMATITIS VENENATA DUE TO MANSONIA WOOD (TERCULIACEA ALTISSIMA). SIBYL HORNER and J. E. M. WIGLEY, Brit. J. Dermat. **48**:26 (Jan.) 1936.

The patient had been a wood-worker (sawyer) in a factory for twenty-five years and had never had any cutaneous eruption until shortly after he began to work with "mansonia walnut," a wood imported from Nigeria.

CHEILITIS ASSOCIATED WITH MICROCYTIC HYPOCHROMATIC ANEMIA. BEATRICE LEWIS, Brit. J. Dermat. **48**:32 (Jan.) 1936.

A woman aged 49 had intractable cheilitis of two years' duration. She was also found to have pallor of the skin and mucous membranes, atrophic glossitis and koilonychia of all the finger-nails. Examination of the blood showed microcytic hypochromatic anemia. The presence of spoon nails was thought to be of great diagnostic significance, and the cheilitis was regarded as an unusual manifestation.

RATTNER, Chicago.

FUNCTION OF THE PIGMENT IN THE SKIN. ROBERT AITKEN, Brit. J. Phys. Med. **10**:30 (June) 1935.

Experimental work is presented to show that pigment in the skin serves as a defense against luminous rather than against ultraviolet radiation.

HARTMAN, Cleveland. [AM. J. DIS. CHILD.]

LEUKAEMIC INFILTRATIONS. J. BURTON CLELAND, Brit. M. J. **2**:1191 (Dec. 21) 1935.

This article, written by a pathologist, discusses the various types of infiltration of tissue with leukemic cells. The infiltrating cells probably reach their location by way of the blood stream and subsequently multiply there. The infiltration is, however, more diffuse than that of an ordinary malignant embolus. Death is usually caused in these cases by secondary anemia and intercurrent infection. In some cases when the kidneys are intensely infiltrated death may result from uremia or from hemorrhage in the brain. Cleland points out that the enlargement of the spleen is not essential in order to arrive at a diagnosis of leukemia and reports several cases.

A man aged 57 died suddenly, exhibiting signs of acute cardiac failure. Postmortem examination showed infiltration of the cardiac muscle and of the tubules of the kidneys by round cells. There was also a large amount of fluid in the pericardial cavity. The liver and spleen were not infiltrated.

A man aged 42 died of severe anemia, dilatation of the heart and early hypostatic pneumonia. Microscopic examination showed round cell infiltrations, with some myelocytes, in the septum and papillary muscle of the heart. The liver also showed a similar infiltration.

A 12 year old school boy died in a "fit" shortly after having been struck on the head by a cricket bat or ball. Postmortem examination showed a large liver and a large spleen, and in sections of the brain there were extensive areas packed with cells of a myeloblastic or myelocytic type. The kidneys and liver were diffusely infiltrated.

An 18 months old child died of a sloughing ulceration of the pharynx, and postmortem examination showed extensive infiltration of the kidneys with myelocytic cells. The pancreas and thymus were also extensively infiltrated.

In the first three cases there was no indication of the leukemic nature of the disease before death.

In 3,500 postmortem examinations Cleland found evidence of the following diseases: myeloid leukemia, 9 cases; myeloblastic leukemia, 4 cases; ordinary lymphatic leukemia, 7 cases; lymphatic leukemia with extensive infiltration, 3 cases; aleukemic leukemia, 3 cases; leukemic infiltration, 4 cases (no blood counts were made in these cases); possible leukemia (atypical), 3 cases; lymphosarcoma, 6 cases; multiple myeloma, 2 cases; chloroma, 1 case; ordinary Hodgkin's disease, 7 cases; acute Hodgkin's disease, 6 cases; Hodgkin's disease with sarcoma, 3 cases.

Four cases of proved leukemia with infiltration are described.

In 1 case there was infiltration of the liver and kidneys with myelocytes and mitoses. In another there were infiltrations at the sites of injections with soamin (sodium para-aminophenylarsonate) and at the site of a surgical incision. In a third case there were lymphatic leukemia, tumor-like infiltrations and nodules in the kidneys, liver and pericardium and plaques on the ribs and spinal canal. In 1 case of lymphatic leukemia there were tumor-like masses around the abdominal aorta, kidneys, mediastinum and left scrotal sac.

In 2 of the cases studied by Cleland there were infiltrations of viscera; in 1 case this was associated with a low and in another with a normal white cell count. Cleland also gives several examples of lymphosarcomatosis and states that no sharp line of demarcation exists between this condition and pseudoleukemia.

This article is illustrated with several photomicrographs of the cellular infiltrations.

APPEL, Boston.

ACRODYNIA AND AVITAMINOSIS. MALDAN-MASSOT, Bull. Soc. de pédiat. de Paris **31**:460 (Nov.) 1933.

A girl 21 months old presented a typical picture of acrodynia. She had been fed nothing but milk and pap. Vegetables, meat juice, calf liver and lemon juice were added to the diet, and after three days the child was markedly improved. On the eighth day from the time she was first observed, administration of 20 drops of a preparation of vitamins A and D and the use of thyroid and adrenal extracts were added to the daily regimen. At the end of a week the child was again examined, and only tachycardia remained of all the signs that were present when she was first observed. The case is reported as an instance which lends weight to the theory that acrodynia is a deficiency disease.

CASE OF RELAPSING ACRODYNIA: STUDIES OF THE VASOMOTOR SYNDROME. B. WEILL-HALLÉ and BORIS KLOTZ, Bull. Soc. de pédiat. de Paris **32**:447 (July) 1934.

A boy 13½ years old presented a typical picture of acrodynia. Most of the cases of this disease which have been reported occurred in much younger children. The patient had marked subconjunctival hemorrhages, without any evidence of other hemorrhage in the body. This case is considered to be the first instance of acrodynia in which this manifestation was present. Another point of interest is that the boy had acrodynia about ten years before, which took about nine months to heal. The duration of the second attack of acrodynia was five months. Injections of acetylcholine and ultraviolet irradiation were used in treatment. These measures

are considered to be of benefit in the treatment of this disease. The sugar, urea and calcium contents of the blood and the sedimentation velocity were normal. Interferometric examination gave normal values for the thyroid and the posterior lobe of the pituitary gland but values higher than normal for the anterior lobe of the pituitary and the thymus, testicle and adrenal. The fact that the boy was at puberty may have influenced these results. The vasomotor system was studied. The peripheral capillaries showed no anatomic abnormalities, but there was functional disturbance: More than the normal number of loops could be seen, and there were stasis and dilatation at the bottom of the loops. The arterial pressure in the retina was found to be elevated during the disease and to be normal later, when the boy had recovered. The oscillometric index was low for all the extremities, and the reactions to heat and cold were abnormal; after the injection of large doses of acetylcholine the index was exceptionally high. Intravenous injection of atropine demonstrated hypersympathicotonia and slight hypovagotonia. In this case definite vasomotor disturbance was shown, as evidenced by stasis of the peripheral capillaries of the extremities and arterial vasoconstriction, associated with hypersympathicotonia. Manifestations of this disturbance were observed as tachycardia, hypertension, especially of the diastolic type, a very low oscillometric index and paradoxical response to immersion of the extremities in a hot bath.

THREE CASES OF MALFORMATION OF THE SKIN OF THE NECK: LATERAL FOLDS OF THE SKIN (PTERYGIUM COLLI CONGENITUM), LATERAL AND POSTERIOR FOLDS AND SUBMAXILLARY DERMATOPTOSIS. MLLE. NAGEOTTE-WILBOUCHEVITCH, Bull. Soc. de pédiat. de Paris **32**:683 (Dec.) 1934.

These observations were made on three women, two aged 19 and one of advanced years and married. None had any abnormality of the vertebrae, although no mention is made of roentgenologic examination. It is believed that the abnormality of the skin of the neck does not appear as a single congenital deformity but is only part of a disturbance probably of endocrine origin. Other abnormal characteristics may be present, such as infantilism, obesity, amenorrhea, congenital defects of the heart, anomalous development of the hair, cutaneous folds on the shoulders and elbows, excessively large ears and various malformations of the face and limbs, all of which may be due to an endocrine disturbance.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

ERYTHRODERMA DESQUAMATIVUM (LEINER-MOUSSOUS DISEASE). P. LEREBOULLET and A. BOHN, Nourrisson **23**:201 (July) 1935.

This report concerns eighteen cases of erythroderma which occurred within a few months among the infants in a hospital for foundlings near Paris. The average duration of the disease was from one to two months, and in no case did a chronic type of infantile eczema result. In a few instances cutaneous abscesses developed as a complication. One patient died of bronchopneumonia. The disease appeared only in infants who were fed artificially. Laboratory investigations showed an excessive number of enterococci both in the stools and in the desquamations of the skin of the babies with the disease. This may be of etiologic significance, though it does not explain why all the cases occurred on one floor of the hospital. Practically all the babies with the disease failed to gain weight normally, and marked anemia developed. Treatment is not discussed.

MCCLELLAND, Cleveland. [AM. J. DIS. CHILD.]

A CASE OF DERMATOMYOSITIS. OLEA G. RICARDO, Arch. Hosp. de Niños Roberto del Rio **5**:78 (June) 1935.

The author reports the rare condition of dermatomyositis in a child over 3 years old. The chief symptoms were swelling and bleeding of the gums and painful swellings about the elbow joints and in the knees and calves of the legs. Considerable edema and erythema developed about the mouth and over the involved

areas of the extremities. Ricardo states that contractures in the extremities are a sequel occasionally. The prognosis is generally good. There is no specific treatment. A diet with high vitamin content is recommended.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

INFLUENCE OF THE SPLEEN ON ALLERGIC CONDITIONS. C. R. GRIEBEL, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:101, 1935.

Griebel reviews the literature on the functions of the spleen and describes his studies of its influence on allergic conditions. He made sugar tolerance tests on rabbits, some of which had first been sensitized by repeated subcutaneous injections of small amounts of an allergen. The allergic animals showed considerable eosinophilia. In tolerance tests it was proved that the metabolism of sugar is disturbed in these animals in that the sugar content of the blood reaches an unusually high level and remains at this high level for much longer periods than it does in animals that have not been made allergic. However, when the allergic animals were given an injection of an extract of spleen (free from protein, sugar and lipoid) before undergoing the sugar tolerance test the reaction was considerably reduced toward the normal. In other experiments the reticulo-endothelial system of the animals was blocked. Griebel concludes that clinical observations as well as experiments on animals indicate that the spleen exerts a considerable influence on the eosinophilic blood picture. It was found that the administration of an extract of spleen in allergic disturbances (bronchial asthma, vasomotor rhinitis and hay fever) produces the best results in vasomotor rhinitis; in hay fever the effects are less favorable, and in bronchial asthma they are least favorable. To be sure, the eosinophilia was reduced in all these conditions, but only in vasomotor rhinitis was this reduction accompanied by a cure. Griebel considers spleen therapy promising in the treatment of allergic disorders.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE TREATMENT OF TUBERCULOSIS OF THE MUCOUS MEMBRANE. O. WARTEMANN, Dermat. Wchnschr. **100**:680 (June 15) 1935.

Wartemann reports good results in the treatment of tuberculosis of the buccal mucosa by means of moderate diathermy followed by painting with a combination of two complex preparations, the first containing calcium carbonate, potassium phenolate and phenol and the second containing salicylic acid, sodium silicate, glycerin, sugar and spermaceti.

CUTANEOUS AND ORGANIC DISEASE AS LATE SYMPTOMS OF INFECTIONS. DEZSÖ VON KÉMERI, Dermat. Wchnschr. **101**:939 (Aug. 3) 1935.

The author discusses the importance of focal infection in relation to cutaneous disorders. Focal infection may cause, or affect the course of, many different conditions, some of which are considered specific.

IMPREGNATION OF THE SKIN WITH ZINC. I. I. POTOTZKI, Dermat. Wchnschr. **101**: 947 (Aug. 3) 1935.

A 32 year old man received a blow near the eye in the course of a fight. The denuded area was dressed with a paste containing zinc which was allowed to remain for twenty-five days. Subsequently multiple white spots were seen in the skin, each surrounded by a telangiectatic network. Chemical investigation showed that the spots were zinc.

ANOTHER CASE OF SYPHILITIC CHANCRE PRESENTING THE PICTURE OF BALANITIS (BALANITIS SPECIFICA SYPHILITICA FOLLMANN). FERDINAND GERENCSÉR, Dermat. Wchnschr. **101**:976 (Aug. 10) 1935.

A case is described in which the chancre was clinically suggestive of balanitis simplex.

CLINICAL OBSERVATIONS ON LEPROSY AND ITS TREATMENT. PETER SUMMENT, Dermat. Wchnschr. **101**:1002 (Aug. 17) 1935.

Summent expresses the belief that leprosy is more common in Europe than is generally believed, especially in Estonia and in Lithuania. He comments on the fact that the method of transmission of the disease is still unknown. In the treatment of leprosy, the usual derivatives of chaulmoogra oil are used. In addition resistant ulcers have been successfully treated with a powder of sulfur and tar.

THE VARICOSE SYMPTOM COMPLEX. WILHELM RICHTER, Dermat. Wchnschr. **101**: 1023 (Aug. 24) 1935.

Richter reviews the "varicose symptom complex" with its various cutaneous manifestations. He also discusses the local and general treatment.

ECZEMA AND HEMOLYTIC JAUNDICE. A. W. DAWIDOW, Dermat. Wchnschr. **101**: 1030 (Aug. 24) 1935.

A 42 year old man entered the clinic for treatment of an eczema which had been present on the face and extremities, showing exacerbations, for twenty years. On examination hemolytic jaundice was found to be associated with the eczema.

A SIMPLE METHOD FOR THE REMOVAL OF TATTOOING. G. H. KLÖVEKORN, Dermat. Wchnschr. **101**:1271 (Oct. 12) 1935.

Klövekorn refers to Janson's article (*Dermat. Wchnschr.* **101**:894 [July 20] 1935) and states that two or three years ago at a clinic in Cologne a patient had a tattoo removed without a scar. The method employed was the daily massage with moistened sodium chloride. The author treated another patient successfully by the same method. The area was rubbed until it became erythematous, and it was necessary to continue this treatment for several months.

TAUSSIG, San Francisco.

FROM "ACRODYNIA" TO "ENCEPHALITIS VEGETATIVA," THE HISTORY OF A DISEASE. PAUL SELTER, Ergebn. d. inn. Med. u. Kinderh. **46**:315, 1934.

Except for the epidemic of acrodynia which occurred in France from 1828 to 1832, the author claims to have first called the attention of the medical world to this disease in 1903, when he described eight cases, designating the condition as "trophodermatoneurosis." The disease is the result of infectious or postinfectious damage of the central nervous system, with striking involvement of the ectoderm and its derivatives.

First, the hands and feet redden and swell, the disorder simulating first degree frost-bite, and this is followed by gross desquamation. The redness involves not only the hands and feet but practically all the terminal parts of the body, such as the nose, ears, cheeks and external genital organs. Sometimes this is preceded by a transient initial exanthem of scarlatiniform, morbilliform or urticarious character. Considerable sweating, unrelated to the intensity of the disease, is a rather constant finding. Paresthesias of all sorts, ranging from anesthesia to hypesthesia and hyperesthesia of a degree which "burns like fire," have been observed by various clinicians. The hair and nails show nutritional disturbances; the hair becomes brittle, dry and lusterless and may change in color, while the nails may break off near the edges and, after the termination of the illness, may show striations similar to the changes following acute infectious diseases, such as scarlet fever. Rarely, the nutritional disturbances of the skin, manifested by the wet, cold and cyanotic extremities, may lead to necrosis or even to gangrene, indicating that one is dealing in this disease with trophic disturbances. Excessive salivation, loss of teeth, occasional vomiting, diarrhea, anorexia, thirst, epigastric pain, hypersecretion from the nose and eyes, the occasional development of keratitis, frequent and marked photophobia, bronchitic phenomena and disturbances of the urine are all symptoms

resulting from involvement of the tissues that are derived from the "ectoblast." The palsy is not complete. It is manifested by fatigue and pain in the extremities, and the patient walks like one suffering from progressive muscular dystrophy. The condition is not true palsy but hypotonia of the muscles. The reflexes may be normal, increased or diminished; similarly, the electrical reactions may vary from one case to another. The circulation of the blood, not the circulatory organs or the blood elements, is disturbed, giving rise to tachycardia as well as to an increase in the blood pressure. Various other disturbances, such as delirium, attacks of cramplike pain, inability to talk and apathy followed by excitability, crying, insomnia, restlessness and a host of other functional irregularities, are observed at various stages of the disease. The temperature is usually normal and may be subnormal; when a complicating infection sets in, the temperature is, of course, elevated. As a result of the anorexia and vomiting, most patients lose considerable weight. The laboratory studies yield negative results. The author states that the pathologic observations are similar to those of encephalomyelitis. The course of the disease varies from three weeks to three years, the usual duration being from two to three months. Most patients recover, the mortality being somewhere between 5 and 6 per cent. The author concludes that the disease is an infection causing injury of the "vegetative cerebral centers," and he therefore calls the disease encephalitis vegetativa.

CAPPER, Philadelphia. [AM. J. DIS. CHILD.]

CASES OF VEGETATIVE NEUROSIS (FEER'S DISEASE). T. VARGA, Orvosi hetil. **79**:379 (April 6) 1935.

Three cases are reported. The first child, aged 3 years, had severe itching of the palms and soles, so that they had to be scratched with a brush, even in the night, and the child could not sleep because of the itching. Other symptoms were also found, such as acrocyanosis, excessive perspiration, hypotonia, decrease of the reflexes, etc. The second child, aged 4 years, had the same symptoms, but the itching was not as severe as in the first case. The third case was that of a 10 year old girl. The illness began with fever, which lasted one week. The typical symptoms of Feer's disease were also to be found, but the mental depression and the disorders of motion and sleep pointed to encephalitis. It seems that there are borderline cases, in which the condition forms a transition between Feer's disease and encephalitis.

GÖTTCHE, Budapest, Hungary. [AM. J. DIS. CHILD.]

PATHOGENESIS OF IMPETIGO CONTAGIOSA ALBOSTAPHYLOGENES (DOHI). H. ASANO, Jap. J. Dermat. & Urol. **38**:792 (Nov.) 1935.

A vesicular eruption consisting of single or multiple translucent, flaccid vesicles from the size of a millet seed to that of a cherry with a meager surrounding inflammatory reaction or none is frequently encountered during the warm, humid months in Japan. It has been studied by the Dohis and others and ascribed to Staphylococcus albus. In the relatively few cases in which Staphylococcus aureus has been the organism encountered it has been dismissed from consideration as merely a secondary invader or part of a mixed infection.

Asano, however, secured Staph. aureus in pure culture in 21.4 per cent of a group of cases of this disorder. By means of parallel studies of Staph. albus and Staph. aureus as to biologic characteristics (coagulation of milk, fermentation of sugars, hemolytic power, culture on crystal violet mediums, agglutination reaction, resistance to acid and to heat, behavior toward antiseptics, such as acriflavine hydrochloride, an acridine derivative and glycerin, toxicity when injected intraperitoneally into rats and toxicity for the skin of rabbits, of guinea-pigs and of puppies) and especially by observation of the results of intracutaneous injection into the skin of the forearms of nursling children, she arrived at the conclusion that in certain cases Staph. aureus may be the sole pathogenic agent. Therefore, she considers the name impetigo contagiosa albostaphylogenes (Dohi) to be inappropriate and

proposes in its stead the name impetigo albo-aureostaphylogenes or impetigo staphylogenes infantum.

Asano found the biologic behavior of the staphylococci of the normal flora of the skin to be identical with that of the staphylococcus causing impetigo. She believes that the reason that these organisms at times invade the subepidermal layers of the skin, producing the typical superficial vesicular lesion of impetigo, may be found in the difficulty in immediately getting rid of the sweat by evaporation. During the late part of the summer humid sultriness prevails in the region of the city of Osaka, where Osana is doing her work, and she believes that alkalinization (formation of ammonia) due to decomposition of the sweat and diminution of the sterilizing effect of drying are favorable to the growth of the staphylococcus. To these climatic factors are added the ease with which minute abrasions are produced in soggy, wet skin and the delicate make-up of the skin of nursling children.

Asano believes that the reason for the scarcity of this condition in nurslings before the fourth month of life lies in the fact that the sweat glands are not fully developed before that time.

J. W. Brennan, Chicago.

A Case of Ulcus Vulvae Acutum with Aphthae-Like Lesions in the Mucous Membranes of the Mouth Associated with Acute Iritis. M. Nishimura, Lues: Bull. Soc. japon. de syph. **12**:149 (June) 1935.

Nishimura reports the case of a 16 year old girl who suddenly became ill with chills, fever and general malaise. On the following day she complained of pruritus and a burning sensation of the vulva; three days later painful ulcerations developed on the labia minora pudendi, and the ulcers gradually became larger. One week later painful lesions developed on the mucous membranes of the mouth and throat.

On the inside of the left labium minus pudendi there was a large, oval, painful ulcer with a slightly undermined soft edge. The base was uneven and covered with a grayish-white purulent material. A similar lesion was seen on the inside of the right labium minus pudendi. Besides these two large lesions there were numerous small erosions on the inner side of the labia minora pudendi and in the vestibulum vaginae. The Wassermann reaction was negative, and bacteriologic examination revealed Bacillus crassus.

The pharynx was congested and the tonsils were swollen. The gums and the uvula showed aphthae-like erosions of irregular shape with sharp edges and erythematous areola. B. crassus was found in these ulcerations also.

Twenty-six days after the onset of the illness an acute iritis developed. The author expresses the belief that this case proves that ulcus vulvae acutum may spread by way of the blood stream and produce a general infection. Until 1927 eighteen cases of ulcus vulvae acutum were described in the Japanese literature.

Bloom, New York.

Lipogranuloma and Adiponecrosis Subcutanea Neonatorum. G. Mosberg and E. Behr, Nederl. tijdschr. v. geneesk. **79**:3050 (June 22) 1935.

Mosberg and Behr observed a case of so-called adiponecrosis subcutanea neonatorum in a boy of 5 weeks. In connection with this case an investigation was made as to the pathogenesis of this disease and its possible connections with so-called lipogranulomatosis. The authors conclude that in the complex of etiologic factors that cause adiponecrosis subcutanea neonatorum an endogenous factor is the prime agent. Trauma has a certain importance as an exogenous cause; in this respect a relationship exists with lipogranulomatosis, in which, however, exogenous factors are predominant. As an important point of difference between these two diseases the chemical process is stressed, which in adiponecrosis subcutanea neonatorum is mainly a deposition of crystallized fats originating from the fatty tissue, whereas in lipogranuloma disintegration of fat occurs. These views could be confirmed experimentally.

van Creveld, Amsterdam, Netherlands. [Am. J. Dis. Child.]

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

FRANK C. COMBES, M.D., *Secretary*

Jan. 7, 1936

MAX SCHEER, M.D., *Chairman*

ROENTGEN RAY DERMATITIS TREATED WITH OINTMENT CONTAINING VIOSTEROL. Presented by DR. BEATRICE KESTEN for DR. ROBERT MCLAUGHLIN.

P. O., a man aged 29, born in Russia, is presented from the Vanderbilt Clinic. He was first seen in 1925. At that time he presented an occupational dermatitis venenata of one year's duration. From 1925 to 1927 he received forty one-fourth unit doses of roentgen radiation to the interdigital areas of each hand, with lead foil shielding. Roentgen rays were applied to the dorsum of the hand only. From 1928 or 1929 to 1931 he received twenty or more additional exposures to roentgen rays, but the hands were exposed from four angles so that the palmar, dorsal, medial and lateral aspects of the hands were exposed to the rays. After he had received fifteen doses in the second series of treatments, the patient noticed that red spots appeared on the skin, but the exposures were continued by the roentgenologist in charge. In 1931 the patient was treated for roentgen ray dermatitis by means of intensive ultraviolet irradiation given at weekly intervals and soaks of sodium thiosulfate applied twice a day. After three months his hands were worse, and he was hospitalized for a few months. At that time zinc oxide appeared to be the cause of his dermatitis venenata, and the acute condition of the hands was relieved by an ointment of lead oleate.

When he was discharged from the hospital the patient was given intravenous injections of liver extract experimentally. He received twenty of these in ten weeks, and much improvement in his general condition and some improvement in the condition of the hands resulted. After the injections were discontinued, his hands became worse again in spite of the fact that the liver therapy was continued orally and subcutaneously.

For the next year or so he was treated with viosterol orally and with boric acid ointment locally, but not much change resulted. In the spring of 1935 he was treated with an herb remedy without appreciable improvement.

In August 1935 treatment was started with an ointment containing about 8 per cent viosterol in a proprietary ointment base. The hands at that time showed a well developed telangiectasia complicated by keratoses, crusting, fissuring and, on the palms, vesiculation and exfoliation. The patient was able to close his hands about one-third but was unable fully to extend the fingers. After three days of the local treatment with viosterol the vesiculation and exfoliation of the palms began to regress, and within three weeks the crusting and vesiculation had disappeared. The patient was able to move his hands normally owing to the improved condition of the skin. At the present time it seems that the keratotic lesions have disappeared in spots and diminished in size in other areas. The patient states that the telangiectases are disappearing, and this is particularly noticeable on the right thumb. The left hand has been treated with the proprietary ointment base alone without viosterol for one week.

DISCUSSION

DR. GEORGE C. ANDREWS: This patient received roentgen irradiation at the old Vanderbilt Clinic; later he went to a private physician, who gave him about fifty roentgen treatments. He came back to the Vanderbilt Clinic later, at which time he had a roentgen ray dermatitis. I think there is no doubt that there has been considerable improvement in the hands owing to the treatment with ointment containing viosterol. As far as I can remember, a year ago the hands were scaly and somewhat keratotic and fissured, and there was more or less stiffening of the joints as well as contracture and atrophy due to lack of use. I think that all these symptoms have improved considerably. The patient is able to move his fingers more freely.

DR. HERMAN FEIT: This case is of the utmost importance because up to now no treatment for roentgen ray dermatitis was known. A few years ago I presented a woman who had complete contracture of the hands together with the superficial changes characteristic of roentgen ray dermatitis. I treated her with viosterol and also with a high vitamin and salt-free diet. The beneficial result was apparent in this woman; she had not been able to close her hands for years, and after she had received the treatment she was able to open and close the hands. I was never able to explain how the salt-free and high vitamin diet could have such an effect. I should like to hear the opinion of Dr. Blumenthal.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation): It is difficult to obtain any improvement in this condition, and the result in the patient presented is remarkable.

DR. HERMAN SHARLIT: I gather from the few remarks which have been made that something can be done for roentgen ray dermatitis. Apparently one may apply vitamins to the skin by means of salves. I should like to hear more about this. Is the treatment truly useful?

DR. E. WILLIAM ABRAMOWITZ: The result obtained in this case is excellent. In carrying out the treatment, it would be wise to treat one hand with the proprietary ointment base alone without the voisterol to see the difference, if any is noticeable, in the results. I should also like to know if any of the members has had any experience with the use of the leaf of Aloe vera that has been reported to be efficacious in treating roentgen ray dermatitis (Collins, C. E., and Collins, Creston: Roentgen Dermatitis Treated with Fresh Whole Leaf of Aloe Vera, *Am. J. Roentgenol.* **33**:396 [March] 1935).

DR. ADOLPH ROSTENBERG: Is the leaf of Aloe vera incorporated in the ointment prepared by a manufacturing company in Buffalo? I had an experience with that salve recently. A patient had a radiation burn about the size of a 25 cent piece; it was not deep but was painful. After about three months of treatment with this ointment the ulcer closed up completely.

DR. GEORGE C. ANDREWS: I think that Dr. Rostenberg refers to an ointment made by Dr. Creston Collins, of the Florida Medical Center, Venice, Fla. It contains extract of Aloe vera in 10, 20 or 40 per cent strength. I have used it and the leaves of Aloe vera extensively on patients with roentgen ray dermatitis and have seen some good results, although I think that in the majority of cases the benefits were no greater than those which would have been obtained by simple dressings moistened with saline solution. However, there is no doubt that the extract of Aloe vera possesses stimulating and healing properties affecting chronic ulcerative roentgen ray dermatitis, and some workers, who have used it more extensively than I, claim that even better results are obtained when the drug is used in early stages of the disorder.

I do not think that one should be too enthusiastic about the result in the patient presented tonight, because, although the hands are decidedly better, the same result might have been obtained by the use of many other preparations.

I have seen some cases of chronic roentgen ray dermatitis in which the telangiectasia tended to disappear after a number of years.

DR. MARION B. SULZBERGER: I agree with Dr. Andrews that one must be cautious in ascribing too much credit to the therapy in this case, particularly as it is known that mild forms of roentgen ray dermatitis, and even some forms in which ulceration is present, show improvement as a result of mild topical remedies, such as, for example, boric acid ointment. Sometimes rapid improvement follows the use of petrolatum alone. One patient, a physician's secretary, with roentgen ray dermatitis of the hands, who had ulcers, keratoses, scaling and telangiectasia, was sent to me about three years ago. Rather haphazardly I gave ultraviolet irradiation to the hands. The patient was so much improved after the first few ultraviolet irradiations that I have continued to give such irradiation once or twice a week during the past three years. There has been marked improvement as a result of this treatment alone; topical applications have not been used. I thought it would be interesting to mention the beneficial effect of the ultraviolet irradiation on the roentgen ray dermatitis in my case, in view of the results with viosterol in Dr. Kesten's patient. Perhaps there is a specific ultraviolet (photochemical) effect to be considered. I shall try to present my patient at a future meeting of the section.

DR. ROBERT MCLAUGHLIN (by invitation): Too much is not being claimed for the treatment used in this case. There are several obvious things to be considered. This man had an occupational dermatitis venenata that may have complicated the picture when this treatment was first started. The idea of using viosterol in the ointment was based on the beneficial effect of ultraviolet irradiation in the treatment of roentgen ray dermatitis obtained by others. In 1933 Drs. Dokforsky and Platt used the same principle in the treatment of acne, but they gave viosterol internally. They thought that the benefits in acne were due to the effect of the viosterol on the skin. In roentgen ray dermatitis the oil glands are totally destroyed, and perhaps some of the effect from ultraviolet radiation has been the application of vitamins A and D to those areas. It is not known whether it is vitamin A or vitamin D that is doing the work; perhaps it is neither. All I can say is that the patient is much better. My co-workers and I will take photographs and follow this case. We hope to show that the telangiectasia is rapidly disappearing. The patient has been observed for results of this treatment for only about four months. The question of spontaneous healing was brought up. The last roentgen treatment was given four years ago, while the healing has occurred in four months. This patient had taken viosterol by mouth for one year. Dr. Abramowitz asked about the advisability of using the proprietary ointment base alone on one hand and viosterol in the ointment on the other. That has been done in the past week only, and I believe that in the daylight a difference can be seen. I hope we shall have opportunity to present this patient again when there will be more conclusive evidence. I do not want to claim value for the treatment yet.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?). Presented by DR. MAX SCHEER.

L. M., a Negress aged 66, is presented because of a generalized eruption of two years' duration. The eruption is most marked on the face, thorax and extremities. It consists of numerous discrete and confluent areas of depigmentation, the largest measuring several inches in diameter. Some of the depigmented areas are covered with an adherent grayish scale. There is considerable scaling throughout the scalp, especially over the vertex. There is an associated moderate alopecia on the vertex of the scalp. The left ulnar nerve is slightly enlarged.

Examination for tinea on Dec. 10, 1935, gave negative results. The results of the Wassermann test of the blood were negative; those of the Kahn test were plus-minus; those of the Kline diagnostic test, 2 plus, and those of the Kline exclusion test, 4 plus.

DISCUSSION

DR. ISADORE ROSEN: I have seen a few similar disorders in Negroes, the early symptoms of which were those of a toxic erythema. After the condition had been present for some time the lesions acquired the clinical features of lupus erythematosus.

DR. HENRY D. NILES: I agree with Dr. Rosen's diagnosis of disseminated lupus erythematosus. Depigmentation is quite common in Negroes with that condition. Dr. Scheer's patient also has lesions on the scalp which are not exactly similar, but which, I think, fit in with the picture.

DR. FRANK C. COMBES: I agree entirely with what Dr. Rosen has said as to the difficulty of distinguishing between acute generalized disseminated lupus erythematosus and erythema multiforme. Sir Norman Walker, I believe, remarked that he knew of no way to differentiate between these two conditions clinically. The depigmentation, of course, is quite characteristic for Negroes. I know of no way to make a definite diagnosis of lupus erythematosus in this case, and the only means of arriving at a probable diagnosis is to study the configuration of the lesions.

DR. MAX SCHEER: Of course, this patient was seen only a month ago, and hence the early manifestations of the disease were not observed. I know nothing about the lesions which appeared two years ago, and I cannot say whether they resembled erythema multiforme or not. Only the depigmentation, some atrophy and slightly scaling lesions remain. The only diagnosis one can now make tentatively from the lesions is that of lupus erythematosus. A biopsy was made today, and the results will be reported at the next meeting.

SARCOID. Presented by DR. LEWIS B. ROBINSON.

Z. H., a Negress aged 42, is presented from the Vanderbilt Clinic. She was previously presented in March and in May 1932. In 1926 she was found to have chronic pulmonary tuberculosis, and at that time she had a negative Wassermann reaction. In February 1932 she was admitted to the clinic with a generalized cutaneous eruption (the appearance is shown in photographs attached to the chart). The Wassermann reaction at that time was 4 plus, and the patient was presented as exhibiting tertiary syphilis. Treatment for syphilis was instituted, but no change occurred in the lesions. In April 1932 a biopsy was made, and the diagnosis was sarcoid. Until January 1933 the patient was treated with preparations of bismuth and of gold. She left the clinic at that time. When she returned in August 1933 she stated that her right foot had been swollen and that she had suffered from hoarseness for one month. All the cutaneous lesions had completely disappeared, their disappearance being coincident with the appearance of hoarseness and swelling of the foot. The reaction to old tuberculin was negative with a 1:10,000 dilution. The diagnosis of tuberculosis of the first metatarsal joint of the right foot and of tuberculous laryngitis was confirmed. In January 1934 a tuberculin test gave strongly positive results. Roentgenograms of the long bones showed no evidence of cyst formation. Those of the chest showed a diffuse peribronchial fibroid tuberculosis of about the same degree as that which was present in 1926.

SARCOID. Presented by DR. LEWIS B. ROBINSON.

E. E. S., a Negress aged 25, is presented from the Vanderbilt Clinic. The patient was presented in December 1932 (**27**:874 [May] 1933). At that time she had lesions on the face which had been present for three years. The reaction to tuberculin was negative. Histologic examination of one of the nodular lesions showed sarcoid of a small nodular type. The lesions at that time appeared to be similar to those which are present now. In May 1932 a roentgenogram of the chest was interpreted as showing evidence of soft extra densities scattered

throughout the pulmonary fields. This was considered consistent with advanced tuberculosis of recent origin. There was pleural thickening at the apex of the right lung. The costophrenic angles were clear.

The patient was treated with a gold preparation (4-amino-2-aurothiophenyl carbonic acid) for approximately a year without much improvement. She also received a salt-free diet for five or six months.

In November 1933 there developed what was probably a tuberculous bronchopneumonia or tuberculous pleurisy with effusion. In March 1934 the patient returned to the clinic, and it was found that all the cutaneous lesions had completely cleared up. Tuberculin tests showed the following results: With a 1:1,000 dilution the immediate reaction consisted of a 1 cm. wheal and the delayed (forty-eight hour) reaction of a 1.5 cm. swollen and red lesion. With a 1:10,000 dilution the immediate reaction consisted of a 0.7 cm. wheal and the delayed (forty-eight hour) reaction of a 1.2 cm. swollen and red lesion.

In November 1935 the patient again returned to the clinic, stating that there had been itching of the eyelids for two weeks previously and that this had been followed by a reappearance of all the cutaneous lesions, the manifestations being as at present.

DISCUSSION

DR. FRED WISE: I recall that Dr. Nomland described a series of disorders similar to that exhibited by this patient. He protested against the diagnosis of disseminated miliary lupus and thought that the diagnosis of sarcoid was more correct. It is my opinion that in disorders like this certain lesions, like the one on the cheek which is discoid, are likely to show the histologic structure of sarcoid, whereas the ones situated around the eyelids, lips and mucocutaneous junctions are likely to resemble disseminated lupus miliaris. This is not surprising, especially in Negroes, in whom both types of histologic picture are frequently obtained when different lesions are examined at the same time. If the diagnosis of sarcoid was made in this case, it is probable that a discoid lesion was examined. I do not think it makes much difference what these individual lesions are called, as they represent different forms of tuberculosis with varying histologic structures.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation): This disorder represents a transition between lupus miliaris and the sarcoid forms, and it would be difficult to make an exact classification. All one can say is that there are a true hematogenous eruption and a high allergic state. In patients with these forms of tuberculosis the reaction to tuberculin may be strongly positive or negative (positive anergy). There has always been discussion as to whether it is necessary to distinguish all these forms of tuberculosis. My opinion is that there are advantages in distinguishing these variations of cutaneous tuberculosis because the clinical and microscopic pictures give the opportunity to draw important conclusions concerning the prognosis and the therapeutic procedure.

DR. T. J. RIORDAN: In a recent review of four cases of disorders of this type at the University Clinic the opinion just expressed by Dr. Wise was substantiated from a histologic standpoint. In other words, there were four cases in which the disorder was diagnosed clinically as miliary lupus, but in two of these cases there was a question as to whether the clinical diagnosis should be sarcoid or miliary lupus, the histologic picture confirming both diagnoses. Two sections from the same patient showed a tuberculous structure in one section and the tuberculoid structure of sarcoid in the other.

DR. EDWARD R. MALONEY: I agree with what Dr. Wise has said. I think one ought to be satisfied with calling this disorder tuberculosis cutis. So many Negro patients with tuberculosis of the skin exhibit different types of lesions—some having typical lesions of lupus miliaris and some sarcoid and sarcoid-like lesions—that I think one cannot apply a name that properly describes such a polymorphous eruption.

DR. MARION B. SULZBERGER: I also agree with what Dr. Blumenthal has said and, as stated by Dr. Wise, in cases of these combined forms it is impossible to make one diagnosis which will embrace all the lesions. However, I agree with Dr. Blumenthal that in every case of tuberculoderma it is essential to try to make as exact a diagnosis of the type of tuberculosis as possible. I think that some of the lesions in this case are typical clinically of lupus miliaris faciei disseminatus. There are other lesions that resemble sarcoid, and still other lesions which somewhat resemble granuloma annulare. It is interesting that the tuberculoderms which this patient presents are of the anergic type. However, she reacted to tuberculin in a 1:1,000 dilution, I believe. This reaction is important, as Dr. Blumenthal said, as far as local resistance to the bacillus and general resistance are concerned. The point which, I think, one learns from disorders of this type is one I have learned only since I came to America; namely, as I have observed and frequently stated, there is a great deal of difference between tuberculosis of the skin in Negroes and that in the white persons. Such unusual combinations of tuberculoderms are much more rarely seen in white persons than in Negroes, and the reactions to tuberculin exhibited by Negroes are often atypical. Negroes generally show transitions from one anergic form to another and combinations of various forms, and they also frequently exhibit transitions between, and combinations of, the sarcoid and the lupus vulgaris types. In white persons such transitions and combinations are rarely seen. This is due, I think, to the well known variations in the racial allergic response to the tuberculous infection and to cutaneous infections in particular.

DR. B. LAPOWSKI: Will Dr. Blumenthal explain in what manner the proper differentiation of tuberculous disorders of the skin, excluding lupus vulgaris, will help to select the correct treatment?

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation): The hematogenous forms of high allergic states can be influenced by therapy much more easily than the localized forms of moderate allergic states like lupus vulgaris. In the first the general treatment with ultraviolet rays and the climatic and dietetic treatment used in the same way as in internal tuberculosis give much better results than in lupus vulgaris.

DR. EUGENE TRAUGOTT BERNSTEIN: I wish to call attention to the work which was done by Herman Pinkus (*Arch. f. Dermat. u. Syph.* **170**:194 [May 31] 1934). He emphasized the complex multiplicity of various forms of atypical tuberculids occurring in one person. There also exists, in rare instances, a vicious circle between cutaneous lesions and pulmonary tuberculosis. In all probability the picture is similar to that observed in asthma and eczema: asthma disappears and eczema appears, or vice versa.

DR. SAMUEL M. PECK: If evaluation of the tuberculin test is to be made it should be done properly. A single test is insufficient, and so is a single dilution. When one talks of several types of lesions of a tuberculous nature in the same patient and discusses the possibility of a transition from one type to another, one of course means that there has occurred in the allergy to tuberculin an actual change which accounts for such a transition. In order properly to study a case in which such a transition occurs, not only must the test be made with several dilutions of tuberculin but it must be made at several sites. It would be difficult for me to believe that a patient who is generally anergic would exhibit lupus vulgaris at one site and sarcoid at another if the hypersensitivity to tuberculin were the same all over the body. Another example can be observed by making repeated tests with the same dilution of tuberculin. At the time when the hematogenous tuberculous lesion resembles lupus vulgaris the reaction to tuberculin may be strongly positive. A short while after, when the sarcoid-like lesions develop, the reaction may be negative. What I wish to bring out is that when the reaction to tuberculin is properly evaluated the fluctuation and change in hypersensitivity to tuberculin can be detected. After all, that is the important information which the test gives.

DR. FRED WISE: There are certain points about which Dr. Peck spoke which I should like to have cleared up. I am almost certain that lupus miliaris disseminatus faciei, as originally described by Colcott Fox, is not the same disease as that which this patient exhibits tonight. It is similar to it, but the distribution and the individual lesions are different. This patient has lesions which are undoubtedly tuberculous. The eruption is almost confined to the mucocutaneous junctions and is not disseminated over the cheeks as is the case in the disease described by Colcott Fox. What is the reaction to tuberculin in the majority of cases of that disease, and how does it compare with the reactions in the disease exhibited by this patient, assuming that the two entities are clinically different? I wonder whether the reactions to tuberculin in this patient would be the same as they would be if the disease were lupus miliaris disseminatus faciei, regardless of the co-existence of lesions of sarcoid, which must change the reaction to tuberculin, as Dr. Peck intimated. I should like to have that point cleared up, if possible.

DR. MARION B. SULZBERGER: Dr. Peck will be able to answer Dr. Wise's question. It is inaccurate to call "lupus miliaris disseminatus" "lupus vulgaris disseminatus," for these two terms refer to what are certainly two entirely different and distinct forms of tuberculosis of the skin. Dr. Peck has compiled the largest statistics on the reaction to tuberculin in patients with lupus disseminatus miliaris faciei. This condition is certainly anergic, as it can be classified in the so-called sarcoid group.

DR. SAMUEL M. PECK: I found that 50 per cent of a large group of patients with lupus miliaris disseminatus faciei exhibited negative reactions to tuberculin in a fairly high concentration. This is a fairly high number of persons showing a negative reaction in association with a cutaneous lesion which is known to be of tuberculous origin and in which, in many cases, tubercle bacilli can be demonstrated. This corroborates what Jadassohn first brought out, namely, that these patients tend to show an anergy to tuberculin. The trouble with the statistics which I published was that in the published cases the reports were based on a single tuberculin test. I am sure that if the tests had been made at different times the trend of the disorder would have been better evaluated. In the cases which I reported the trend was toward a negative reaction. The disorder exhibited by Dr. Robinson's patient does not resemble lupus miliaris disseminatus faciei clinically.

DR. LEWIS B. ROBINSON: This patient was first presented with a diagnosis of lupus miliaris disseminatus faciei. Subsequently a biopsy showed typical sarcoid. She is presented because of her history during the last two years. She responded to no therapy for a year. After an attack of pleurisy with effusion, which was regarded as a tuberculous pleurisy, all the lesions immediately disappeared. They did not reappear until a year later.

I presented another patient with a similar disorder. This second patient was presented before the section over three years ago, at which time she had multiple serpiginous lesions thought to be due to syphilis because the Wassermann reaction was 4 plus. That patient failed to show any response to active antisyphilitic treatment for a year. The biopsy showed sarcoid. There developed a tuberculous periostitis of a metatarsal bone of the foot and tuberculous laryngitis. Within a month all lesions on the body disappeared. That patient exhibited a negative reaction to tuberculin, but at the time she had a periosteal lesion the reaction became markedly positive. It is of interest that both of these patients while they had sarcoid showed no signs of active tuberculosis. However, as soon as the tuberculosis became active the sarcoids disappeared. This, I believe, demonstrates that the sarcoid occurs during the anergic phase of tuberculosis and disappears when positive allergy to tuberculin is present.

A Case for Diagnosis (Papulonecrotic Tuberculid?). Presented by Dr. Frank Vero.

W. J. J., a Negro aged 35, born in the United States, is presented from the Vanderbilt Clinic because of an eruption of the skin and swelling of the right side of the neck of four months' duration. The swelling in the neck developed suddenly, and the cutaneous eruption appeared shortly afterward.

There are numerous brownish-reddish papules, from the size of a pinhead to that of a pea; some show slight scaling; others show small necrotic areas in the center. There is a marked cervical adenitis on the right side.

The Wassermann reaction of the blood was negative. Roentgenograms of the chest showed no abnormalities. A biopsy was reported on by Dr. Gerald F. Machacek as follows: Histologically the disorder is either a papulonecrotic tuberculid or a tertiary syphilitic ulceration. The ultimate diagnosis depends on clinical evidence.

DISCUSSION

Dr. Charles Wolf: This case is rather interesting in view of the fact that the Wassermann reaction is negative and that the patient has two pathognomonic signs of late syphilis. He has leukoderma colli and a gummatous infiltration of the right sternocleidomastoid region. These two manifestations are rather resistant to early improvement under antisyphilitic treatment. The other lesions, I think, are not tuberculids but are probably papular urticarial lesions.

Dr. Isadore Rosen: Another diagnosis that should be considered is that of Hodgkin's disease. It is unusual to see such a widespread dissemination of lesions associated with papulonecrotic tuberculids. Another unusual feature is the enlargement of the glands in the neck. This manifestation of tuberculosis is usually found much earlier in life. I therefore suggest that roentgenograms of the chest be made for evidence of mediastinal glandular enlargement and that further studies be made to rule out a disease of the hematopoietic system.

Dr. Frank Vero: This patient was originally referred to the surgical department of the Presbyterian Hospital for diagnosis of the condition of his neck. The disorder was thoroughly studied in both the medical and the surgical departments, where several diagnoses have been considered: first a diagnosis of actinomycosis; then one of abscess of the neck, and finally one of lymphadenitis tuberculosa. Syphilis has not been considered, and the patient has received no antisyphilitic treatment. Wassermann tests have all given negative results. The diagnosis of Hodgkin's disease was not considered. Repeated blood counts have given negative results except for the fact that the hemoglobin content was 68 per cent. The patient was referred to the dermatologic department on account of an eruption involving the neck, both axillae and the lower portions of the legs. The eruption on the neck was follicular and pustular, and I first made a diagnosis of folliculitis due to some pyogenic organism. The eruption in the axillae and on the legs appeared entirely different from that on the neck. The lesions were papular, raised and reddish brown; some had necrotic centers, resolving gradually and leaving pitted scars as seen in typical papulonecrotic tuberculids. A biopsy was made from a lesion on the leg, and Dr. Machacek considered the disorder to be papulonecrotic tuberculid or possibly tertiary syphilis. The patient had recently received two roentgen treatments to the neck; the last one, I think, was given two days ago. The gland on the neck has enlarged considerably since.

Symmetrical Anomaly of the Nails. Presented by Dr. Paul Gross.

A. B., a woman aged 26, is presented from the Hospital for Joint Diseases. The patient remembers having had the condition of the nails for at least ten years and dryness of the skin for about six years. Her father is a physician and has a similar condition of the nails of both thumbs and forefingers. Four brothers and two sisters show no abnormalities in the nails.

The nails of both thumbs show deep transverse grooves and grayish transverse superficial fissures. These changes are confined to the middle portions of the nails throughout their entire length, giving a streaklike appearance. The skin of the corresponding basal portions of the nails appears hyperkeratotic. There are slight furrows in the central portions of the nails of both index fingers. The palms show coarseness of the skin and increased markings, a feature unusual for the hands of a person doing only a small amount of housework and no laundry work. There are a follicular keratosis of the legs and ichthyosis-like scaling on the knees and elbows. The condition of the skin and of the palms is suggestive of ichthyosis.

ACTINOMYCOSIS OF THE JAW (CURED). Presented by DR. BEATRICE KESTEN.

M. H., a Negress aged 37, is presented from the Vanderbilt Clinic. She was presented on Jan. 2, 1935 (ARCH. DERMAT. & SYPH. **32**:503 [Sept.] 1935). She had been admitted to the Presbyterian Hospital on Dec. 4, 1934, because of swelling of the left side of the face of eight weeks' duration. The swelling had occurred after extraction of a tooth. The patient then presented the typical suppurating lumpy jaw with involvement of the mandible and skin of the entire left cheek and upper part of the neck seen in actinomycosis. She was unable to open her mouth more than 1 cm. Actinomyces was found in the pus and grown in culture.

The patient was given 25 drops of saturated solution of potassium iodide but an intolerance soon developed. She then received 150 roentgens (160 kilovolts) of radiation filtered with 1 mm. of aluminum at a distance of 25 cm., six treatments being given at weekly intervals and inhalations of ethyl iodide for three weeks, totaling 30 cc. Four infected teeth were removed, and fluctuating abscesses were incised.

The patient received no treatment for six months and has remained well. Culture of material from the tonsils for Actinomyces on Nov. 22, 1935, gave negative results.

NEW YORK DERMATOLOGICAL SOCIETY

EUGENE F. TRAUB, M.D., *Secretary*

Jan. 28, 1936

RAY H. RULISON, M.D., *President*

DERMATITIS HERPETIFORMIS (DUHRING). Presented by DR. J. FRANK FRASER.

J. R., an American boy aged 8 years, was first seen on May 20, 1935, exhibiting a generalized eruption which had been present for one year. It began on the legs and back and has spread to the chest, neck and face. The lips are also involved. The initial lesions were small vesicles. There is intense pruritus.

Urinalysis gave negative results. The blood cell count showed 4,400,000 red cells, 18,800 white cells and 70 per cent hemoglobin. The differential count showed 68 per cent polymorphonuclear leukocytes, 21 per cent lymphocytes, 7 per cent mononuclear leukocytes, 4 per cent eosinophils and no basophils. The red cells showed a slight decrease in size. A smear from a vesicle showed 12 polymorphonuclear leukocytes to 1 eosinophil. Allergy tests with potassium iodide in 25 and 50 per cent solutions gave negative results. Determination of the basal metabolic rate was ordered, but the internist considered it inadvisable to make the test at this time. Biopsy of a vesicular lesion on the shoulder was reported to show Duhring's disease.

Treatment has consisted of soothing lotions, packs of weak solution of potassium permanganate and roentgen radiation. On Dec. 31, 1935, the patient received

one-quarter skin unit of unfiltered radiation to the chest, back, neck, lips and upper portion of the arms. On Jan. 7 and 16, 1936, he received another one-quarter skin unit of radiation to the affected areas. Some improvement has resulted from roentgen therapy.

DISCUSSION

DR. HENRY H. WHITEHOUSE: I think that the diagnosis of dermatitis herpetiformis is the most logical one. Eruptions in the mouth and on the lips are rather unusual, but the itching, the grouping and the recurring attacks indicate that the disorder is Duhring's disease rather than pemphigus. A number of teeth have been removed, but I understand that the eruption appeared before the teeth were extracted. In consideration of the itching, the distribution and the grouping, I agree with the diagnosis.

DR. A. BENSON CANNON: I agree with the opinion expressed by Dr. Whitehouse, although I am more in favor of the diagnosis of erythema multiforme because of the location of the eruption, the edematous character of the lesions, the involvement of the mucous membranes of the lips, the absence of itching and the youth of the patient. I suggest that the patient be given liver orally and injections of liver extract every other day or even daily. Dr. Rhodes, of the Rockefeller Institute, expressed the belief that in many cases these bullous lesions of the mucous membranes are due to a vitamin deficiency, and he has obtained splendid results in some cases by giving large amounts of liver extract.

DR. HOWARD FOX: In my opinion this patient presents the classic signs and symptoms of Duhring's disease, namely polymorphism, grouping, itching and a tendency to relapse. The presence of oral lesions does not exclude Duhring's disease, though it must be admitted that oral bullae are much less common in that disorder than in pemphigus. I do not think that a diagnosis of pemphigus should be considered as there are no bullae on the cutaneous surface.

(Dr. Fred Wise, Dr. Edward R. Maloney, Dr. Frank Combes and Dr. Eugene F. Traub agreed with the diagnosis of Duhring's disease.)

A CASE FOR DIAGNOSIS (ROSACEA-LIKE TUBERCULID? ROSACEA? LUPUS ERYTHEMATOSUS?). Presented by DR. EUGENE F. TRAUB.

Mrs. M. M., a housewife aged 28, born in the United States, complains of an eruption on the face which first appeared in June 1935. She states positively that she did not suffer an acute sunburn, but she believes that the heat or possibly slight exposure to the sun's rays may have been a factor in causing the disorder. Two other factors which the patient thinks may have been precipitating causes were the sudden and accidental death of her husband and the death of her baby which occurred directly after delivery. These events have made her exceedingly nervous, and in view of the fact that one of the diagnoses first considered was that of rosacea, these events may actually have played a part in the etiology.

The lesions are arranged somewhat in a butterfly fashion on the cheeks and nose. The individual lesions, however, do not suggest lupus erythematosus. They are difficult to describe because it is hard to determine their exact type. At times they seem to be pure papules or tiny nodules, while at other times they appear to be slightly pustular. In the two or three weeks that the patient was under observation there was little response to treatment. There is no history of ingestion of drugs. Tests with tuberculin in graded dilutions gave moderately positive results in the more concentrated dilutions.

DISCUSSION

DR. HOWARD FOX: The clinical diagnosis in this case is, I think, extremely difficult. The disorder does not have the appearance of ordinary rosacea, and there is no history of gastro-intestinal disturbance, which is so common in that disease. The diagnosis seems to lie between lupus erythematosus and some form of tuberculosis.

DR. JOSEPH J. ELLER: I am more inclined to regard the condition as lupus vulgaris than as lupus erythematosus.

DR. J. FRANK FRASER: The diagnosis lies between lupus erythematosus and true tuberculosis.

DR. A. BENSON CANNON: I favor the diagnosis of tuberculosis. The yellow color of the nodules and the crusting are more suggestive of lupus vulgaris than of lupus erythematosus.

DR. EDWARD R. MALONEY: I cannot make a diagnosis in this case. The disorder is either lupus erythematosus or tuberculosis.

DR. HENRY H. WHITEHOUSE: I think it is difficult to diagnose this disorder on the basis of the clinical observations, and the location of the lesions makes it rather hard to obtain material for a biopsy. Clinically I cannot distinguish the condition from lupus erythematosus. If material for a biopsy can be obtained, microscopic studies might be helpful.

DR. EUGENE F. TRAUB: My first idea was that the disorder was plain rosacea. In view of certain features, and particularly because of the associated seborrhea, I gave the patient one or two doses of the roentgen rays of one-quarter skin unit each. It is my opinion that the eruption as seen today is worse than it was before. While I know that rosacea does not always respond favorably to roentgen therapy, I do not believe that the flare-ups are usually as pronounced as is the case in rosacea-like tuberculid. In all cases of this type which I have seen the disorder has always been much aggravated after treatment with the roentgen rays. For this reason the diagnosis that I now favor is that of rosacea-like tuberculid.

ACRODERMATITIS CONTINUA (HALLOPEAU). Presented by DR. A. BENSON CANNON.

S. N., a man aged 25, is presented from the New York City Hospital. He sustained an injury to the right index finger at the age of 2 years, which resulted in loss of the nail. Since the onset of the condition all the other fingers, the palmar and dorsal surfaces of both hands and the nails and plantar surface of the left foot have gradually become involved. There is a definite history of trauma accompanying each new spread of the disease. The patient had received little treatment until eight years ago, when he was given a series of eight roentgen treatments over a period of two years without benefit. He was then given a course of eight injections of arsphenamine, eight injections of a bismuth preparation and three injections of mercury as a therapeutic test, although the Wassermann reaction of the blood was negative at that time. These injections caused all the lesions to clear, but the nails showed no improvement, and since that time the condition has gradually returned. On several occasions the patient had been told that his only hope for a cure was to have all the infected fingers amputated.

There are lesions on the first and second fingers of the right hand, on the second, third and fourth fingers of the left hand, on the dorsal and palmar surfaces of both hands up to the wrist joint and on the third, fourth and fifth toes, interspaces and anterior half of the plantar surface of the left foot. The lesions are definitely demarcated, having a raised overhanging border, beyond which the skin is normal. They are covered with thick, brown scales, the peeling off of which reveals a smooth, red base in which there are numerous pinhead-sized white pustules. The nails are for the most part absent, only rudiments of the nail keratin remaining on several of the affected fingers and toes. The nail beds are covered with scales. Under the scales the base is smooth and contains white pustules like those which are present on the palm and back of the hand.

The Wassermann reaction of the blood was negative. Chemical examination of the blood, urinalysis and determination of the arsenic content of the urine gave negative results. Culture from the margin of the lesion showed Staphylococcus albus. Blood serum gave a negative agglutination reaction for this organism. Roentgenograms of the hands and feet showed small bony spicules coming off

the base of the terminal phalanges of the involved digits. Roentgen examination of the heart, lungs, gastro-intestinal tract and gallbladder showed no abnormalities.

Generalized ultraviolet irradiation and local irradiation to the hands and feet were given twice a week. Autogenous vaccine was given twice a week in gradually increasing doses. Typhoid vaccine was given once a week for six weeks; the therapy caused the temperature to rise to 103.4 F. for from eight to ten hours. The patient was given colloidal manganese once each week. After the administration of typhoid vaccine was discontinued 5 cc. of sterile cow's milk was injected once a week; this caused the temperature to rise to an average of 102 F. for five or six hours on each occasion. The hands and feet were soaked in solution of potassium permanganate twice each day for an hour. Each night for the first two weeks a 10 per cent solution of salicylic acid in olive oil was applied. Twice each week the scales were removed and all visible pustules were opened. The patient has received a high vitamin, high caloric diet.

Steady improvement was noted from the day the treatment was begun; this was particularly evident after each paroxysm of fever. The number of pustules became less numerous each week; the scales became less prominent, and finally normal epithelium appeared in islands throughout the involved area; in time it joined to cover all the previously involved areas, the nail beds being the last to recover.

The patient is presented to show the excellent therapeutic results.

DISCUSSION

DR. EUGENE F. TRAUB: I have been much interested in this patient for many years, and I wish to congratulate Dr. Cannon on the excellent result he has obtained. Certainly at no time since the onset of the disease has this young man's skin been in as good condition as it is today. He was in the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for months, and although some improvement always resulted from treatment a cure was never approached, and in fact I had almost come to believe that the condition was incurable. The patient should be grateful for the result achieved.

A CASE FOR DIAGNOSIS (DERMATOPHYTOSIS WITH DERMATOPHYTID? SCLERODERMA?). Presented by DR. EUGENE F. TRAUB.

R. S., a woman aged 46, born in Russia, was first seen on Jan. 6, 1936, presenting an eruption of four months' duration on the inner aspect of the lower portion of the right leg. The surface was slightly erythematous, and there was a deep, almost boardlike mass in the subcutaneous tissue. The skin covering the involved area could be wrinkled and did not seem to be particularly hidebound.

The Wassermann and Kahn tests and urinalysis gave negative results. The results of mycologic examinations were as follows: The reaction to trichophytin was 4 plus; that to oidiomycin was 3 plus on the patient's arms. A positive wheal reaction appeared about twenty minutes later on the affected leg, and at the site of injection a nodular mass appeared, which remained for at least five or six days. Examinations for tinea gave the following results: Smears from the first, third and fourth interdigital spaces of the right hand and the first and third interdigital spaces of the left hand were all negative; those from the fourth and fifth toe-nails of both feet were positive for mycelia; those of the fifth toe-nail of the right foot were suspicious, and those of the fourth toe-nail of the right foot were negative.

The biopsy report was as follows: The microscopic diagnosis was scleroderma. Aside from a moderate telangiectasia throughout the cutis there was little of importance to be seen. The epidermis showed little change; the basal cell margin was intact, and the granular layer was present throughout. Throughout the subcutaneous tissue were numerous coil glands, several of which were tremendously dilated. The vessels in the fat region were somewhat thickened, and there was marked irritation of the fat. The elastic tissue was intact.

DISCUSSION

DR. JOSEPH J. ELLER: I do not think that the disorder is scleroderma. It might fit into the clinical description of periphlebitis nodularis necroticans.

DR. J. FRANK FRASER: I cannot make a diagnosis.

DR. HOWARD FOX: As the histologic examination shows no evidence of scleroderma, that diagnosis must be excluded. One should consider the possibility of an erythema nodosum-like eruption due to fungous infection.

DR. EDWARD R. MALONEY: I do not believe that the disorder is scleroderma or erythema nodosum. It may be due to some low grade infection which has become manifest as a localized lymphangitis.

DR. FRANK C. COMBES: I do not see how any one can be expected to make a diagnosis in this case on the basis of the presentation. I understand that the lesions are noninflammatory. The picture at present does not suggest scleroderma. There is marked inflammation, probably as a result of the removal of a section of skin for histologic examination. There does not seem to be any evidence of hidebound skin over the involved area.

DR. HENRY H. WHITEHOUSE: I cannot make a diagnosis.

DR. EUGENE F. TRAUB: An examination of the section of skin removed from the center of this lesion seemed to rule out the diagnosis of scleroderma. Whether the disorder can be termed an "id" or not, I am not prepared to say positively. It may be merely a peculiar type of lymph stasis, but as other cases of lymph stasis have been observed in which tinea apparently played a definite rôle, it may be a factor in this case as well. Trichophytin injected into an unaffected portion of the skin of the leg produced a lesion somewhat similar to the one now present. In cases in which there was a positive reaction for tinea associated with an "id", the latter has always cleared up coincidentally with the clearing up of focal infection of the feet with tinea. The treatment of tinea has been deferred so that the eruption would not be altered before the patient was presented. I shall report at a later meeting whether or not the lesion on the leg has responded to this type of therapy.

PARAPSORIASIS VARIOLIFORMIS. Presented by DR. FRED WISE.

E. S., a woman aged 41, was presented before the Section of Dermatology and Syphilology of the New York Academy of Medicine in October 1934. She is presented again because of the interest attaching to a recurrence of the varioliform type of parapsoriasis, associated with lesions of the usual form of pityriasis lichenoides chronica. The eruption disappeared during the summer of 1935, when the patient was exposed to the sun's rays on the beach; it recurred at the end of the summer. The eruption exhibited tonight is of several months' duration.

Brownish red lenticular spots are disseminated over the trunk and limbs; they are slightly infiltrated and covered with a dry adherent scale. Besides these typical lesions there are also a few frankly vesicular lesions and several small superficial ulcers, the sites of previous vesicular lesions.

The Wassermann and the Kahn test were negative. The histologic examination showed parapsoriasis.

DISCUSSION

DR. HENRY H. WHITEHOUSE: The diagnosis of parapsoriasis varioliformis is the best diagnosis I can make on the basis of the clinical appearance.

DR. EUGENE F. TRAUB: I agree with the diagnosis as presented; this patient shows practically all the various types of lesions characteristic of this condition. The disorder apparently responds to ultraviolet irradiation or exposure to the sun's rays; or the remissions that are observed from time to time may be spontaneous and occur in the usual course of the disease.

DR. FRANK C. COMBES: I agree with Dr. Traub.

DR. A. BENSON CANNON: The disorder is interesting, and the lesions are so strikingly similar to those found in psoriasis that I should think it would be interesting to follow the patient, if possible, over a period of several years in order to see whether psoriasis does not develop. The stippling of the nails is also suggestive of psoriasis.

DR. FRED WISE: When this patient was first presented, practically all the lesions were vesicular. Now she presents lesions of scaling parapsoriasis together with vesicular lesions.

SCLERODERMA. Presented by DR. EUGENE F. TRAUB.

E. D., a man aged 52, born in the United States, was first seen on Jan. 22, 1936. The patient states that he had never had any cutaneous trouble until October 1931. At that time he first noticed thickening of the skin on the left side of the abdomen. Later he began having pains in all the joints of both lower extremities. This was diagnosed as arthritis and has been followed by some deformity of the toes and stiffness of the feet, so that walking became difficult. About three years ago the patient began to notice increasing areas of thickening of the skin; these appeared first on the shoulders and within six months involved the chest, abdomen, legs, thighs and arms.

On the anterior aspect of the chest and abdomen, on the arms as far as the elbows, on the legs up to the knees, on the anterior aspect of the thighs, on the hands and feet and on the back are areas of erythematous woody deep-seated lesions with slight scaling. On the hands and feet are areas of secondary infection. The fingers show little movement and are rigidly flexed.

Chemical examination of the blood on Jan. 20, 1936, showed 113 mg. of sugar and 28 mg. of urea nitrogen per hundred cubic centimeters. The Wassermann reaction has been repeatedly negative. Roentgenograms of the skull, pituitary gland, adrenal glands and chest showed no abnormalities. Those of the bones showed trophic changes and atrophy due to disuse. There is a history of ingestion of arsenic, and arsenic was found in the urine.

The patient has been treated by Dr. Rubin with thyroid, potassium permanganate and salves.

DISCUSSION

DR. HENRY H. WHITEHOUSE: The condition of the hands is an unusual feature, but of course the disorder is scleroderma.

DR. A. BENSON CANNON: I have been much interested in the work that has been done by physicians working at the Cornell Medical Center in removing the parathyroid glands in cases of scleroderma. They report that excellent results follow removal of a portion of the parathyroid tissue. They have also obtained splendid improvement in cases of scleroderma by giving injections of calcium. I suggest that the patient be put in proper physical condition for operation, the secondary infection of the hands be cleared up and then a parathyroidectomy be performed. Certainly, his pitiful state calls for radical treatment.

DR. J. FRANK FRASER: I have observed only one case in which a parathyroidectomy was performed. There was no improvement in the condition when the patient was discharged from the hospital.

A CASE FOR DIAGNOSIS (MYCOSIS FUNGOIDES *Homme Rouge?*). Presented by DR. FRED WISE.

H. H., a man aged 53, states that the onset of his disease occurred in March 1935 in the form of diffuse redness and itching of the hands and forearms. This attack cleared up after topical remedies were applied, but the disorder recurred with increased intensity in October 1935. The redness and itching then rapidly spread up the arms and gradually involved the skin of the entire body and of the face.

There is a uniform diffuse dusky red eruption affecting all parts of the body but somewhat less marked on the chest than elsewhere. The skin is smooth and

noninfiltrated on the trunk and face, but the hands and forearms present a moderate grade of thickening and hyperkeratosis, while the palms and soles are definitely hyperkeratotic. The skin of the face is almost purplish red, resembling extremely weather-beaten skin. There are no marks of scratching, but the patient complains of moderate itching, especially at night.

The histologic picture is that of an early stage of mycosis fungoides.

NOTE.—Subsequent examination, on June 3, 1936, revealed innumerable nodular infiltrations from the size of a pea to that of a hazelnut scattered all over the torso and presenting the typical appearance of granuloma fungoides.

DISCUSSION

DR. HENRY H. WHITEHOUSE: I agree with the diagnosis of mycosis fungoides.

DR. EUGENE F. TRAUB: This is the first time that I have seen mycosis fungoides begin in this manner. Though cases in which such an onset occurred have been recorded, they appear to be exceedingly rare in this country. The only lesion that I observed on the patient which would have suggested mycosis fungoides to me is a plaque in the left axilla which definitely shows a certain amount of infiltration and a suggestion of a horseshoe configuration.

DR. FRANK C. COMBES: I agree with the diagnosis as presented. An interesting point is the pallor in the axillae and about the nipples. Such pallor is of frequent occurrence in cases of erythroderma. I have never come to any conclusion as to its significance.

DR. J. FRANK FRASER: This is the *homme rouge* type of mycosis fungoides, and the clinical diagnosis can frequently be confirmed by microscopic examination.

DR. A. BENSON CANNON: I could not make a diagnosis of mycosis fungoides in this case, and I doubt that that disease is present even though the histologic picture indicates it. All I could possibly see was that the patient had a generalized dermatitis. I think that the patient should be thoroughly studied in regard to metallic poisoning or contact dermatitis.

DR. FRED WISE: In view of the histologic report by Drs. Satenstein and Sachs it is probable that the eruption is an example of the *homme rouge* type of mycosis fungoides described by French authors.

ALOPECIA TOTALIS; MILIA OF THE EYELIDS. Presented by DR. FRED WISE.

A. T., a man aged 21, born in the United States, states that he has suffered from loss of hair since the age of 2½ years. The disease began as a patchy alopecia of the scalp associated with loss of eyebrows and eyelashes following an attack of measles at the age of 2½ years. The disease progressed steadily, and complete loss of mature and lanugo hair occurred six months ago. Milia of the upper eyelids also appeared after the attack of measles in infancy.

Roentgenograms of the skull revealed a normal pituitary gland. The basal metabolic rate, the arsenic content of the urine and the dextrose tolerance were all normal. The Wassermann and the Kahn test were negative.

The patient exhibits obvious symptoms of endocrine imbalance, the most evident being excessive obesity and an extension of the skin of the scrotum to form a hood-shaped arch over the root of the penis on its dorsal aspect. The testes appear to be normal but are retracted upward toward the inguinal ring.

DISCUSSION

DR. HOWARD FOX: In my opinion further treatment with anterior pituitary extract (antuitrin) is inadvisable. Like many other physicians, I have given this remedy a reasonably thorough trial in cases of alopecia areata and have never seen the slightest benefit result from its use. I have heard expressions of similar opinion from colleagues in different parts of the country. I think it is important that the negative results obtained by the members of this society be put on record in order to prevent further waste of time and money on the part of patients.

DR. J. FRANK FRASER: I suggest that a spectroscopic analysis be made to determine the presence of metals.

DR. JOSEPH J. ELLER: I agree with Dr. Fox that the therapy with anterior pituitary extract (antuitrin) has not proved to be what it was claimed. I have tried it and have obtained no results so far. This patient's basal metabolic rate is reported to be normal, but clinically there is a definite dysfunction of the pituitary gland and possibly of the thyroid gland. Regardless of the basal metabolic rate, my advice is to give this patient pituitary and thyroid extracts.

DR. EDWARD R. MALONEY: I do not think that the aforementioned gonadotropic hormone is of any value in this type of disorder.

NAEVUS PIGMENTOSUS (MELANOMA). Presented by DR. J. FRANK FRASER.

H. G., a youth aged 17, was previously presented before the Manhattan Dermatologic Society.

The patient is presented for suggestions as to therapy.

DISCUSSION

DR. EUGENE F. TRAUB: I believe it can be stated without a doubt that the lesion is a nevus, but whether it is an ordinary pigmented nevus or a blue nevus I find it difficult to say after a mere inspection. At present the growth certainly seems to be benign, but because it is located where it is more or less constantly subjected to pressure and possible trauma, I believe it is most advisable to remove it in the hope of preventing a future malignant change.

DR. HENRY H. WHITEHOUSE: I cannot say whether the nevus is benign or malignant. I should hesitate to remove it surgically.

DR. HOWARD FOX: I believe that the lesion is a benign melanoma. My advice would be to excise it as it is subject to constant trauma.

DR. JOSEPH J. ELLER: I was under the impression that a blue nevus was level with the skin. The only way to make a final diagnosis is by microscopic examination. I should not treat the nevus as a benign lesion.

DR. A. BENSON CANNON: While I believe that the lesion is a benign blue nevus, I should like to call attention to the possibility of its being an angioma. I have records of two cases in which competent physicians had made a diagnosis of melanoma and in which on removal the growth was found to be an angioma. I do not believe that I have ever seen a soft fluctuating tumor in the center of a pigmented nevus such as this patient presents.

DR. EUGENE F. TRAUB: I have carefully read the description of what a blue nevus should look like. Unfortunately the color is not necessarily a deep blue, but according to Tièche, depending on the depth of the lesion, on the natural color of the patient's skin, on the location and probably on other factors, the color may even be a brownish or blackish blue. For this reason I do not see how it is possible on clinical inspection to distinguish a blue nevus from an ordinary slate-black mole. As the cells of the blue nevus are similar to those constituting a mongolian pigmented spot, I believe that blue nevi become malignant less frequently than other types of pigmented nevi. When one does become malignant it is supposed to develop into a melanosarcoma, in contradistinction to the ordinary pigmented nevus which becomes a melanocarcinoma. In this case I do not believe that the lesion is a vascular nevus of any type, although, I repeat that it is impossible to determine this with certainty on clinical grounds alone. In this location and because of the pressure to which the lesion is subjected I can easily conceive that a vascular lesion might take on the appearance of the present one.

DR. EDWARD R. MALONEY: I should say that this condition is a benign melanoma. The elevated part of the lesion may suggest angioma, but certainly the border is a pigmented lesion.

DR. FRED WISE: I agree with the diagnosis of benign melanoma. Because of its location, I believe it is best to remove the lesion, as there is a possibility of its becoming traumatized. I should remove it by wide and deep excision.

DR. J. FRANK FRASER: I have nothing to add. I am thankful for suggestions as to treatment.

ACNE VARIOLIFORMIS. Presented by DR. EUGENE F. TRAUB.

G. W., a man aged 36, born in the United States, had a typical papulonecrotic eruption for from ten to fifteen years; at times the condition practically cleared up. The lesions appear in crops, being scattered over various areas of the face and scalp and being particularly noticeable about the margins of the hair and the nose. The chief reason for presenting the patient is that the resultant scars are much larger than those usually seen in this disease, some of them measuring from 5 to 6 mm. in diameter and having a depth of from 1 to 2 mm. Such large scars appear to indicate that the active lesions have also been unusually large, and this seems definitely to be the case.

Tuberculin tests gave negative results with 1:1,000,000 and 1:100,000 dilutions and a plus-minus reaction with a 1:10,000 dilution. The condition was made worse by treatment with tuberculin. The biopsy showed a low grade pustule and changes not incompatible with the diagnosis of acne varioliformis.

DISCUSSION

DR. A. BENSON CANNON: While I believe that the condition is suggestive of acne varioliformis I have never seen such terrific scarring and such large and crater-like scars as this patient presents, especially over the nose, to result from acne varioliformis. There are no active lesions that are suggestive of that disease. The few early lesions that the patient has are nothing more than blood-crusted edematous papules. Unless the condition has been thoroughly investigated, I should suggest that this patient be observed with a view to the possibility of the condition's being self-inflicted.

DR. EUGENE F. TRAUB: I admit that I did not consider the diagnosis of neurotic excoriations in this case, and therefore the patient was not particularly studied with this thought in mind. However, I have known the patient for a number of years and at no time has he impressed me as a neurotic person. The lesions are too uniform, and the pitting is of the type seen only after smallpox, chickenpox, acne varioliformis, papulonecrotic tuberculid or similar disease in which all lesions result in deep pits of practically uniform size. The reason I presented the patient was because I thought that the disorder was exceedingly typical, the only unusual feature being the large size of the lesions and the scars resulting therefrom.

REPORT ON A CASE PREVIOUSLY PRESENTED. DR. EUGENE F. TRAUB.

L. C., a woman aged 26, was presented for diagnosis before this society on Dec. 17, 1935 (ARCH. DERMAT. & SYPH. **34:** 534 [Sept.] 1936). The eruption was present on both legs. Endamoeba histolytica was found in the stools. An examination of the urine revealed 3.3 mg. of sodium bromide per hundred cubic centimeters. No iodides were found. When examinations were made in the Massachusetts General Hospital the results of examinations for bromide and iodide content of the urine were said to be negative. In view of the fact that in the discussion one or two of the members mentioned the possibility of an eruption due to a drug I think that this finding is of importance.

REPORT ON A CASE PREVIOUSLY PRESENTED. DR. EUGENE F. TRAUB.

A. O., a man aged 35, was presented before this society on Nov. 26, 1935 (ARCH. DERMAT. & SYPH. **34:** 525 [Sept.] 1936), with a diagnosis of papulonecrotic tuberculid and granuloma annulare.

I wish to recall this patient's condition to the minds of the members. The condition was diagnosed as an extensive granuloma annulare involving the arms

and shoulders, a few scattered lesions being also present on the thighs and on the trunk. The patient also had an eruption which was thought to be a papulonecrotic tuberculid, but this may have been an error, as the latter lesions seemed to undergo spontaneous involution with scarring while the patient was under observation. The patient was given one dose of seven-eighths skin unit of filtered roentgen rays to the granuloma annulare lesions. These have all disappeared, apparently as a result of this treatment.

MINNESOTA DERMATOLOGICAL SOCIETY

F. W. LYNCH, *Secretary*

Feb. 7, 1936

L. H. WINER, M.D., *President, Presiding*

LICHEN PLANUS OF THE EYELIDS. Presented by DR. H. E. MICHELSON, Minneapolis.

A woman aged 29 is presented because of a retiform melanosis confined to the eyelids. The rest of the skin and the mucous membrane are not involved. The biopsy specimen showed changes characteristic of lichen planus. Four roentgen treatments have been administered, and considerable improvement has resulted.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: Dr. Michelson's case is a duplicate of one presented in Chicago, in which he also made the diagnosis of lichen planus of the eyelids.

LYMPHOGRANULOMA VENEREUM. Presented by DR. JOHN F. MADDEN, St. Paul.

M. C., a Negro laborer aged 45, noticed a bilateral painful inguinal adenitis about five weeks ago. The nodes became matted and grew progressively larger and more painful. The patient had sexual intercourse with a Negro prostitute in the latter part of November 1935. No penile lesion was noted. The nodes in each inguinal region are the size of a fist and contain a large amount of pus. The patient complains of constipation and extreme pain on defecation, but proctoscopic examination gave negative results. Ducrey bacilli were not found in the pus; Frei tests and Wassermann examinations of the blood gave repeatedly negative results.

A CASE FOR DIAGNOSIS (LYMPHOGRANULOMA VENEREUM?); PENILE CHANCRE; MACULAR ERUPTION OF SECONDARY SYPHILIS. Presented by DR. JOHN F. MADDEN, St. Paul.

E. J., a laborer aged 35, was first seen on Jan. 10, 1936, presenting a superficial ulcer at the urethral meatus which was indurated and exuded serum. The ulcer appeared five days after intercourse with a prostitute. A bilateral tender inguinal adenitis was present, the glands being from the size of an olive to that of small hen's egg. The patient stated that the adenitis appeared a day or two before he noticed the penile ulcer. There was a slight urethral discharge, which was present throughout. The ulcer and adenitis remained about the same for from four to five weeks. About the beginning of the fifth week the penile ulcer began to enlarge, and a massive edema of the prepuce appeared. The first Frei test gave negative results. Each of the remaining tests showed an increasing reaction. No Ducrey bacilli were found, and smears showed no gonococci. Repeated dark field examinations for Spirochaeta pallida gave negative results. The Wassermann reaction of the blood was positive on Feb. 7, 1936 (about the seventh week after the onset of the adenitis), and a macular eruption of secondary syphilis appeared on the skin at that time.

LYMPHOGRANULOMA VENEREUM. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. J. R., aged 25, first complained of a painful induration and edema of both labia majora and of an inguinal adenitis on the left side on Nov. 20, 1935. She was first seen at the hospital on Dec. 6, 1935, when the gland was incised and drained. There was no history or evidence of a primary ulcer. The patient had had sexual intercourse with her husband shortly before the edema and adenitis were noted. The husband had a penile ulcer and inguinal adenitis at that time. The Wassermann reaction of the blood was repeatedly negative. Several smears showed no gonococci or Ducrey bacilli. The Frei reaction was moderately positive on Dec. 8, 1935, and it has been strongly positive since Jan. 1, 1936.

LYMPHOGRANULOMA VENEREUM. Presented by DR. JOHN F. MADDEN, St. Paul.

J. R., a laborer aged 30, was first seen on Oct. 1, 1935, at which time he presented a painful fluctuant inguinal bubo on the left side and a pea-sized painless ulcer of a week and a half duration on the middle of the dorsal aspect of the prepuce. There was also a bean-sized, firm nodule to the left of the midline about half-way up the shaft of the penis. The patient stated that he noticed a urethral discharge about one month previously and that this was followed in a few days by the inguinal adenitis. The bubo was incised, but the disease continued to progress until the patient was admitted to the hospital on Dec. 17, 1935. Repeated dark field examinations of material from the ulcer gave negative results for spirochetes. No gonococci or Ducrey bacilli were found on repeated examinations. The first Frei test on November 26 gave a positive reaction, and since then there has been a more marked reaction to each test.

DISCUSSION

DR. R. J. BAILEY, Rochester (by invitation): At the Mayo Clinic my co-workers and I have attempted to make comparative studies with the various Frei antigens. Dr. Welsh recently obtained from Dr. J. Tamura Frei antigen, cultured virus of lymphogranuloma venereum and antilymphogranuloma venereum serum. In the few patients on whom we have made comparative intradermal tests the cultured virus gave the most marked reaction. Tamura Frei antigen, Cook County Frei antigen (furnished by Dr. Wien) and Lederle Frei antigen all gave positive results but to a lesser degree.

In one case, that of a young man from South America who had a marked stricture of the rectum of several years' duration, desensitization was started with the Cook County antigen. Within three weeks improvement proceeded to the point where a proctoscope could be inserted. This brings up the point, which has been verified by postmortem examination, that the stricture is not entirely cicatricial but is caused in part by the marked round cell infiltrate; the latter infiltrate may resolve as a result of biologic therapy.

The virus has been cultivated through several animal passages by Dr. Tamura.

DR. HAMILTON MONTGOMERY, Rochester: I wish to emphasize what Dr. Michelson has already said, namely, that not all lesions in the groin or axilla are to be regarded as caused by lymphogranuloma venereum. At one time false positive reactions to the Frei test were obtained.

A patient presented at a recent meeting of the Chicago Dermatological Society exhibited a condition which clinically was at first suspected of being lymphogranuloma venereum with involvement of both axillae, the groin and other regions, but further investigation proved that the disease was extensive tuberculosis.

DR. JOHN F. MADDEN, St. Paul: My co-workers and I made several interesting observations on our patients with lymphogranuloma venereum. Two of the patients noticed a urethral discharge from one to two weeks before the inguinal adenitis appeared. Although the discharge was examined repeatedly, no gonococci were ever found. We attempted desensitization with antigen, roentgen therapy, intravenous administration of neoarsphenamine and medication with antimony and potassium tartrate in conjunction with incision and drainage of the fluctuant buboes.

As long as our patients were ambulatory no form of treatment seemed to benefit them. When they were kept in bed and treated with hot packs and small doses of filtered roentgen radiation steady improvement occurred.

CONTACT DERMATITIS FROM OVERSHOES. Presented by DR. JOHN F. MADDEN, St. Paul.

LIPEMIA-XANTHOMA. Presented by DR. D. D. TURNACLIFF, Minneapolis.

H. B., a man aged 23, whose height is 5 ft. 2½ inches (1.59 meters) at present weighs 157 pounds (72 Kg.). Four years ago he weighed 183 pounds (83 Kg.). He has lichen simplex chronicus on his left leg; this is not associated with the condition because of which he is presented.

The patient has always been of the same stature and "gets fat" easily. He is the only member of his family who exhibits this tendency.

About three years ago there developed three lesions of xanthoma on the right palm and right foot. At about that time the patient was advised to reduce, and he gradually took off weight until he weighed 150 pounds (68 Kg.). The lesions remain stationary. When I first saw the patient six weeks ago I suggested that he increase his weight 4 or 5 pounds (1.8 or 2.3 Kg.) before an examination of the blood was made. One week ago examination gave the following results: lipoids, 1,360 mg.; cholesterol, 603 mg., and sugar, 107 mg. per hundred cubic centimeters of blood.

This is about twice the normal amount. To make sure that the results did not represent a normal increase in fat content of the blood due to increase in weight, I recently examined blood from an obese man weighing 280 pounds (127 Kg.) who had gained 30 pounds (13.6 Kg.) in four weeks, and the lipoid content of his blood was normal.

Further evidence of pituitary disorder is the fact that in this man the growth of hairs associated with sexual development is lacking, although his genitalia are normal.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis: Little is actually known concerning the pathogenesis of xanthoma. The lesions may occur in persons having increased cholesterol content of the blood or in persons having a normal amount of cholesterol. Increase in lipoid content of the blood does not necessarily parallel gain in body weight.

DR. HAMILTON MONTGOMERY, Rochester: Dermatologists tend to narrow the concept of xanthoma. There are all types of xanthomatosis, including also the Schiller-Christian syndrome. Xanthomatous lesions may be seen in the larynx and pharynx, even independently of any cutaneous manifestations. They should be searched for whenever the question of xanthomatosis of any type arises.

DR. D. D. TURNACLIFF, Minneapolis: When the patient weighed about 180 pounds he probably had a marked excess of lipoid in the blood. It is my impression that patients with this disorder have so much lipoid in their blood serum that it crowds through the capillaries.

The members may remember that last year I presented a man with several hundred lesions of xanthoma which cleared up completely when the fat content of the blood was reduced through dieting (ARCH. DERMAT. & SYPH. **33**:898 [May] 1936; **34**:320 [Aug.] 1936). It is conceivable, if a lesion of xanthoma persists for some time, that enough fibrosis takes place so that a reduction of the fat content of the blood will not cause the lesion to recede.

Would it not be conceivable that diabetic patients go through a period of lipemia and that the lesions of xanthoma develop during that period?

I was glad to have the opportunity to check the lipoid content of the blood on the man weighing 280 pounds because the results of that examination will perhaps classify the lipemia group more definitely with dysfunctions of fat metabolism.

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W. NISBET, M.D., *Secretary*

Feb. 9, 1936

NELSON PAUL ANDERSON, M.D., *Chairman*

DISSEMINATED LUPUS VULGARIS. Presented by DR. SAUL S. ROBINSON.

XANTHOMATOSIS. Presented by DR. STANLEY CHAMBERS.

The patient's illness dates back about three years. At that time a swelling in the legs was noticed; swelling of the forearms and upper portions of the arms gradually developed; later the tissues of the face, chest and back became involved. There has been some loss of function of the hands associated with the tumor-like masses on the forearms. The patient states he has been treated in several clinics and by private physicians since the condition was first noted.

There is a yellowish plaquelike waxy infiltrative involvement of the entire head, which is more marked over the supra-orbital areas of the forehead and the bridge of nose. The same type of involvement is present in the areas generally affected by seborrhea, the anterior aspect of the sternum, the back and the arms. There are several hard masses on the forearms and upper portions of the arms.

On Jan. 7, 1936, the Wassermann reaction of the blood was negative, and chemical examination of the blood gave the following results: nonprotein nitrogen, 38.7 mg. per hundred cubic centimeters; urea nitrogen, 19 mg.; sugar, 102.6 mg.; calcium, 11.8 mg., and cholesterol, 151.5 mg. The icteric index was 13.8. The van den Bergh reaction was negative.

On Jan. 6, 1936, the report on a roentgen examination was as follows: There was no evidence of pathologic changes in the right and left forearm and wrist. There were no apparent calcium deposits within the soft tissue.

The biopsy report stated that the specimen consisted of a piece of skin from the forehead, the epidermis of which did not show. The dermis, however, contained islands of polyhedral cells and oval cells, rather closely placed, with a comparatively small nucleus, eccentrically placed. The cytoplasm was foamy. The cells were probably endothelial leukocytes. There was an occasional giant type cell. The diagnosis based on microscopic examination was xanthoma.

DISCUSSION

DR. SAUL S. ROBINSON: I suggest the diagnosis of leprosy. There seems to be muscular atrophy.

DR. C. R. HALLORAN: The clinical picture is that of leprosy. I suggest that further studies be made with this thought in mind.

DR. MOSES SCHOLTZ: If the diagnosis is correct, this is an interesting case. My first suspicion was leprosy, a diagnosis which, I think, should be considered. "Xanthomatosis" is not a clear term. Does it mean degeneration of the skin or toxic xanthoma? The lesions are entirely too superficial and too extensive to represent degeneration of the skin. In many places there is wrinkling of the skin. I suggest an alternative diagnosis of chronic dermatitis atrophicans with secondary xanthomatous deposits.

DR. IRVING R. BANCROFT: I think that the diagnosis of leprosy should be considered.

DR. H. C. L. LINDSAY: I noticed that one eyebrow was partly missing, but it would take time to make a definite diagnosis.

DR. KENDAL FROST: I agree with Dr. Scholtz. I should not presume to question the diagnosis after the extensive investigation which has been made. The clinical picture is different from any type of xanthoma which one ordinarily sees and is interesting.

Dr. William H. Goeckerman: Dr. Frost has expressed my opinion. I understand that the case has been studied thoroughly. If xanthomatosis proves to be the correct diagnosis, a report of the case ought to be sent to the international congress.

Dr. Samuel Ayres Jr.: I have never seen any clinical picture like the one in this case. I agree with the remarks which have been made, and I second the suggestion that the patient may present xanthomatous changes associated with some other disorder. Whether leprosy could produce that change, I do not know, but clinically that diagnosis is the first thing suggested by the patient's appearance. There are areas of definite infiltration of a sclerodermatous type as well as areas of atrophy where the skin is like tissue paper and atrophic in appearance. Certainly the case is highly interesting.

Dr. Stanley Chambers: Xanthomatosis is, of course, a pathologic entity which is probably better understood by biochemists and pathologists than by dermatologists. My conception of the disease has always been a clinical one, yet if one appreciates step by step the pathogenesis of the disease, the picture which this patient exhibits becomes logical and makes one wonder why it is not seen more frequently. I know of no other disease which produces the pathologic changes so evident in this case. Xanthoma or foam cells are pathognomonic of the disease. The sections presented tonight show great numbers of these characteristic cells. Repeated examination of nasal smears showed no evidence of leprosy. Dr. Paul O'Leary and his associates at the Mayo Clinic studied this case. The diagnosis at that time was xanthomatosis.

Dermatitis Factitia. Presented by Dr. Moses Scholtz.

MANHATTAN DERMATOLOGICAL SOCIETY

Mihran B. Parounagian, M.D., *Secretary*

Feb. 11, 1936

Paul E. Bechet, M.D., *Chairman*

A Case for Diagnosis: (Erysipeloid?). Presented by Dr. Fred Wise.

G. R., a boy aged 10 months, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of a recurrent eruption of seven weeks' duration. The present attack occurred about five days ago. The previous history, including that of birth and past illnesses, is essentially irrelevant.

The eruption is widespread and involves the buttocks, lower extremities, hands, feet and prepuce. The pubic region and groins are not affected, but a band about 6 inches (15 cm.) wide spreads across the entire width of the abdomen. The affected parts are diffusely erythematous, slightly edematous, dry and in some parts, especially on the lower portion of the back and on the abdomen, covered with dry adherent thin lamellar scales. The other areas are quite shiny and sharply marginated. There is no photophobia, polyneuritis or paresthesia. There is a daily rise of temperature to 101 F., coincident with a flare-up of the eruption. The rash is said to vanish almost completely every day and to reappear at fairly regular daily intervals. The sharp margin of the eruption on the abdomen seems to coincide with the upper edge of the adjusted diaper. The thenar regions of both palms exhibit sharply marginated flat smooth and glistening patches of dermatitis, and the soles are similarly affected, except that the dermatitis involves the entire plantar surfaces.

DISCUSSION

DR. ANDREW J. GILMOUR: If the child had more fever I might suggest the diagnosis of an erysipeloid eruption.

DR. MIHRAN B. PAROUNAGIAN: I have never seen any disorder like that before, so I cannot make a diagnosis.

DR. LUDWIG OULMANN: The disorder may be an allergy to alkaline substances. Acrodynia can easily be excluded, and an erysipeloid condition would be deeper seated.

DR. HOWARD FOX: Some of the lesions on the soles suggest a diffuse syphilid, but the rest of the eruption does not at all resemble that disease, and I think it can be excluded. If it were not for the lesions on the hands, erythema gluteale might be considered.

PERIVASCULITIS NODULARIS NECROTICANS. Presented by DR. FRED WISE.

F. M., a woman aged 27, from the clinic of the French Hospital first complained of her cutaneous trouble last December, when she was exposed to cold weather. The lower third of the right leg, chiefly the frontal and lateral aspects, presented a series of from twenty-five to thirty well defined flat discoid soft nodules, varying in size from that of a pea to that of a dime and showing a range of color from light pink to violaceous. Some of the lesions exhibited faint superficial erosions in their centers. They were painful and tender. The intervening skin was cyanotic and cold.

The patient had infantile paralysis in childhood, and she wears a brace on the affected leg. On the external surface of the right heel and outer malleolus is an elongated postoperative scar resulting from a bone graft performed in an attempt to correct her disability.

Her general health is said to be quite normal. There are no clinical evidences of active tuberculosis and no other cutaneous lesions. Tests with tuberculin will be made later.

DISCUSSION

DR. LUDWIG OULMANN: From a purely clinical standpoint periphlebitis nodularis necroticans cannot be differentiated from a possible tuberculid; a biopsy and tuberculin tests are necessary to establish the diagnosis.

DR. MIHRAN B. PAROUNAGIAN: Clinically I should agree with Dr. Oulmann's suggestion that the disease may be tuberculid.

DR. PAUL E. BECHET: In my opinion the disorder belongs to the tuberculid group. The fact that it occurs only on one leg does not refute such a diagnosis. The lesions are on the deformed and shrunken leg and may well have developed there because of the lowered resistance of the leg to infection or disease as well as because of a lowered circulation. Is periphlebitis nodularis necroticans a clinical entity, or is it an atypical type of Bazin's disease? Certainly some of its manifestations are entirely different from those of erythema induratum or any other known dermatosis. Some years ago I observed two cases of an exactly similar clinical syndrome, namely, subcutaneous nodules or small tumors arranged in beadlike formation on the lower third of the leg. The nodules were deep and hard and did not fluctuate. They were reddened but not painful and seemed attached to the subcutaneous tissue. They did not break down, but in the course of several months disappeared, leaving a brownish discoloration and a depressed area. They did not resemble Boeck's sarcoid in the least, nor could they be regarded as lesions of erythema nodosum.

FAVUS OF THE SCALP AND NAILS. Presented by DR. FRED WISE.

L. S., a woman aged 24, an accountant, was born in the United States. Her eruption began on the scalp eighteen years ago. The patient had two epilations with roentgen rays ten and four years ago, respectively. The eruption involving the fifth finger-nail of the right hand and that involving the third finger of the

left hand began three and two years ago, respectively. The patient received ten treatments with roentgen rays to the affected nails one year ago.

There is a grayish yellow discoloration affecting the aforementioned nails together with a moderate subungual hyperkeratosis. The nail of the left middle finger is broken off at about the middle. The distal portion of the nail bed is grayish white. There is a severe grade of alopecia affecting the entire scalp; it is most marked over the central portion and is associated with moderate scaling. The scrapings as well as the cultures from the finger-nails and from the scalp showed the organism of favus.

The Wassermann, Kahn and Kline tests were negative.

A Case for Diagnosis (Lupus Erythematosus?). Presented by Dr. Andrew J. Gilmour.

E. H., a man aged 25, single, born in Ireland, is an attendant in a hospital. He has always been well except for the fact that he had lichen planus in 1932. The trunk and extremities were extensively involved, and on these locations pigmentation remained several months. The mouth was slightly involved.

Since it first became involved the mouth has never been quite normal. There has been a blue-red color extending back from the angles of the mouth. These two lines followed the approximation of the teeth for 1 inch (2.5 cm.) on each side of the mucous membrane of the mouth. This line was from ½ to ¾ inch (1.2 to 2 cm.) in width, level with the surface and not ulcerated. No sensation to food was elicited. The teeth were not rough.

Since the middle of December 1935 there have been on the right side of the exposed portion of the mucous membrane of the lower lip two slightly raised hyperkeratotic lesions each ½ inch in diameter. These have been scaly and gray; they were never ulcerated or covered with scabs.

The Wassermann test was negative.

DISCUSSION

Dr. Fred Wise: I think that this eruption is lupus erythematosus.

Dr. Howard Fox: I agree entirely with Dr. Wise, and I can see no reason for considering the disorder an epithelioma. I suggest treatment with a gold preparation.

Lupus Erythematosus. Presented by Dr. Howard Fox.

D. D., aged 35, a Negro, has suffered from a lesion on the scalp for the past three years. On the vertex is an oval patch about 7 inches (18 cm.) in the longest dimension, which is red, dry, atrophic and devoid of hair. Since the patient was admitted to the hospital he has had frequent crops of flaccid bullae on the affected area. No cause for these eruptions has been found.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Vaughn C. Garner, M.D., *Secretary*

Feb. 21, 1936

Herbert J. Smith, M.D., *Chairman*

Dermatitis Medicamentosa Due to Barbiturate. Presented by Dr. John B. Ludy.

H. J., a woman aged 37, presents an outbreak of small papules on a purpuric background. She states that she took sleeping tablets (dial) after a severe emotional upset. Four days ago a generalized pruritic eruption appeared suddenly. The patient's skin is purplish in cold weather. There is no history of rheumatic fever, tuberculosis or other infections. There is marked dental sepsis.

DISCUSSION

DR. MARION B. SULZBERGER, New York: I think that one of the main things to remember about eruptions due to drugs is that they can take all forms, no matter what the drug is that causes them. The typical eruptions are only those which are most frequently caused by one certain drug. In other words, while the most common eruption due to phenolphthalein is the fixed eruption, that drug does not necessarily cause only fixed eruptions. Bromides may cause not only acneiform or fungating, but also eczematous, seborrheic and occasionally fixed eruptions. In this case I think that it is difficult to make a differential diagnosis between an eruption due to bromide and one due to barbiturate. I understand that the patient has taken both drugs. The fact that many of the lesions are follicular makes me suspect that the causative drug may be a bromide; it is known that eruptions due to bromides are often follicular. There are acneiform lesions on the chest, back and face, which would point more to a halogen as the cause of the eruption, and hemorrhagic and purpuric eruptions such as that exhibited by this patient may develop from ingestion of bromides. Therefore, while it is possible that the barbiturate may have caused all the lesions, I think that the bromide must be considered also.

DR. JOHN H. STOKES: In commenting on eruptions due to a drug I always say that that diagnosis is a last rather than a first resort. One should carefully eliminate every other explanation before one attempts to incriminate a drug. I think that rule should be applied even in the case of drugs which are known to produce distinctive and characteristic eruptions because I have seen some of the most egregious mistakes made in dermatologic practice by systematically attributing eruptions which follow intake of drugs to the drugs. I do not think there is any worse *post hoc ergo propter hoc* practice than the tendency to call an eruption which appears after a patient receives a drug an eruption due to a drug. Purpura is due to a drug only when it is proved to be so, and a painstaking and systematic study of this patient's disorder should be made before it is called an eruption due to barbiturates, bromides or any other drug. There prevails at present an epidemic infection of some sort which manifests itself in a large number of persons by gastro-intestinal disturbances and which, I am convinced, is causing a flare-up of pyogenic infections of the skin by a sensitizing process. I think that infection will be responsible for some toxic erythemas. I should not be at all surprised if in some cases purpura results from it. The fact that a person is taking a barbiturate at the time a purpura appears does not justify a diagnosis of eruption due to a drug.

DR. WILLIAM O. ROOP, Atlantic City, N. J.: The eruption on this patient's face is an acne rosacea, and she admits that this eruption was present for quite a long time before the generalized eruption which now involves the body. In my opinion the eruption on the body resembles more an eruption due to barbituric acid than one due to a bromide.

DR. EDWARD F. CORSON: It seems to me that the sudden onset and the generalized distribution point to barbituric acid rather than to bromide as a cause.

A CASE FOR DIAGNOSIS (NEURODERMATITIS? PREMYCOTIC STAGE OF MYCOSIS FUNGOIDES?). Presented by DR. LOUIS GOLDSTEIN.

H. L., a man aged 26, presents a generalized eruption of a patchy, papular and desquamating character varying in shape, color and process of involution. Certain parts show definite infiltration, especially at the upper part of the thighs and in the region of the axillae, where there are distinct ribbon-like raised borders. The inguinal glands are markedly enlarged. A moderate pruritus is present more or less constantly. The condition has been present for three months. It began on the legs as a papular dermatitis after the patient wore woolen stockings (contact dermatitis?) and rapidly progressed to the rest of the body. Early in the course of the disease the dermatitis of the legs developed into an inflammatory edema with exudation, while the rest of the body presented a purplish papulation which

gradually formed various-shaped patches as well as extensive desquamation. About seven weeks ago there appeared on the chest and trunk papular lesions suggestive of a superimposed pityriasis rosea. These became confluent and finally evolved into the stage of dermatitis existing at present. The Wassermann reaction of the blood was negative. Chemical examination of the blood gave normal results. The blood count showed a moderate leukocytosis, the number of leukocytes being 10,000, and a corresponding increase of polymorphonuclear leukocytes. Urinalysis gave negative results.

DISCUSSION

DR. FRANK C. KNOWLES: I cannot diagnose this eruption.

DR. FRED D. WEIDMAN: I cannot make a diagnosis at present. I think that the case will have to be investigated.

DR. FRANK C. KNOWLES: Some of the lesions certainly resemble tinea imbricata. I think further studies in regard to fungous origin should be made.

DR. FRED D. WEIDMAN: I do not believe that the disorder is tinea imbricata or generalized dermatophytosis; it is more probably mycosis fungoides. Neurodermatitis can be definitely excluded.

DR. MARION B. SULZBERGER, New York: I cannot make a diagnosis either. Naturally, the first thing one thinks of on seeing the isolated patches is a tinea, and I think that this diagnosis must be excluded by repeated careful mycologic examination. I have seen recently a tinea resembling this patient's eruption; in that case there was generalized lymphadenopathy, and the fungi could be demonstrated. On the other hand, in a case of an eruption somewhat similar to that presented by this patient repeated examinations for tinea gave negative results. I do not believe that neurodermatitis need be considered; I do not know what type of neurodermatitis this could be. The way the eruption has spread from the calves, the fact that the lesions are fairly uniform, that the eruption is nonhemorrhagic and that it always spreads centrifugally suggest tinea which is becoming generalized. I do not think that mycosis fungoides ever starts in one place and spreads from there. As a rule, in mycosis fungoides there are multiple lesions beginning in various parts of the skin.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I think that possibly the disorder is a type of leukemia.

DR. SIGMUND S. GREENBAUM: On morphologic grounds I should diagnose it as plain eczema. I do not know whether it is a premycotic eczema or whether it is due to a chemical from within or without or to a parasite, but the picture now is that of a straight eczema. I must confess, however, that I incline quite strongly to the belief that the eruption is due to a fungus. I think Dr. Sulzberger has summarized the arguments cogently for that diagnosis. It is known, however, that in scrapings the organism may not be found even though morphologically there may be evidence of a fungous eruption.

DR. LOUIS GOLDSTEIN: I wish to ask Dr. Sulzberger if the patient would have so much itching and such extensive scaling from a fungous infection.

DR. MARION B. SULZBERGER, New York: My experience is that these generalized atypical fungous infections are often atypical in more ways than one. It is not at all unusual for severe itching to occur in a fungous infection. I have seen cases of fungous infections of the feet in which itching was the outstanding symptom. As far as the scaling is concerned, in cases of widespread involvement the patches often do not come to full development but remain scaling. I think that the entire picture in this case could well be of fungous origin, but this diagnosis requires confirmation by laboratory examination.

DR. JOHN H. STOKES: I should like to point out that itching is much like pain in that it is a function of the individual threshold of sensory responsiveness. Some persons may have itching due to a lesion between the toes and tear themselves frantically, while others may have an extensive eruption of which they are

quite unaware. That is apparent in cases of scabies. The threshold of itch in scabies varies with the patient and not with the extent or character of the disorder. I remember the case of a physician with a typical mycosis fungoides; annular infiltrated lesions were developing, and the patient had had the premycotic stage for eighteen years, but he swore that he had never had any itching. Such observations are familiar. I think one becomes convinced after a while that itching is a function of the individual nervous system and of the individual reactivity quite as much as, if not more than, of the eruption.

A Case for Diagnosis (Chronic Aphthae? Erythema Multiforme?). Presented by Dr. Herman Beerman.

G. S., a man aged 33, was presented at the October 1935 meeting of the society (Arch. Dermat. & Syph. **33**:760 [April] 1936). Aside from the oral lesions he has two small ulcers on the scrotum. The diagnoses of chronic aphthae, eruption due to phenolphthalein and erythema multiforme have been considered.

The differential blood cell count showed 7,200 white cells with 63 per cent polymorphonuclears, 30 per cent lymphocytes, 3 per cent monocytes, 1 per cent eosinophils and 3 per cent transitional forms. Urinalysis gave negative results. Serologic tests of the blood gave negative results on three occasions. A smear from the tongue showed no spirilla, but there were some small round bodies resembling yeasts which may have been mouth contaminants. The Pels-Macht test showed a phytotoxic index of 65. The patient was treated with brewer's yeast, 10 drops of dilute hydrochloric acid three times a day, 60 grains (0.39 Gm.) of calcium lactate three times a day, sodium perborate locally and five injections of whole blood. He received eight injections of neoarsphenamine from Oct. 1 to Dec. 2, 1935, the first dose being 0.3 Gm. and the following doses 0.45 Gm. During observation of the patient several lapses were noted. After initial improvement had occurred, on Aug. 20, 1935, the patient reported that two days previously he had had a rather marked exacerbation of lesions in the mouth and on the scrotum. This relapse lasted about two weeks. After three weeks of relative freedom from complaints, on September 24, several eroded ulcers were noted on the scrotum and penis. During the time neoarsphenamine was given it seemed that there was marked improvement, but on December 2, the date of the last injection, two new ulcers appeared, one on the left side of the buccal mucosa and one on the palate.

DISCUSSION

Dr. Sigmund S. Greenbaum: I have recently observed several cases, and there have been a number reported in the literature, in which these chronic aphthae have been the result of an idiosyncrasy for certain foods. I suggest that the patient be tested with food allergens though the results are likely to be negative, or that he be put on an elimination diet—the latter procedure is usually more successful.

Dr. John H. Stokes: I may point out that one way of achieving a result in a supposedly allergic process of this sort seems to be to increase the intake of vitamins, especially that of vitamin B, which has a therapeutic effect and an influence on intestinal infection and intestinal absorptive power. That treatment was used coincidentally with the neoarsphenamine, and yesterday my co-workers and I agreed that we were not sure whether the vitamins or the neoarsphenamine had caused the improvement. Improvement as a result of treatment with neoarsphenamine was much greater than it had been as a result of the combined therapy, however, and consequently we were inclined to think that the arsenic had made some difference. But certainly the allergic background should be investigated.

Dermatitis Herpetiformis. Presented by Dr. John B. Ludy.

D. H., a man aged 44, says that eighteen months ago a red slightly scaly eruption appeared on one knee and shortly spread, slightly involving the buttocks, the elbows, the dorsal aspect of the arms and the shoulders. In June 1935 the character of the eruption changed abruptly with the onset of a vesicular eruption

similar to the existing outbreak. There were violent itching and burning. Arsenic controlled the eruption for a number of months. On Feb. 10, 1936, calcium gluconate was substituted for the arsenic. On the evening of February 11 the patient went to a dance but ingested nothing but chocolate cake and nonalcoholic punch. The next morning there was a profuse eruption which was symmetrical and consisted mostly of bullae and of an erythema multiforme type of outbreak with festooned and circinate lesions, best exemplified in the region of the groins and on the lower portion of the back. Some of the latter lesions are of the herpes iris type. The axillae are crowded with vesicles. The face has been involved only in the recent attack. There are no lesions on the mucous membrane. The patient had carbuncles five years ago. His tonsils have not been removed. He has no sinus trouble, is not constipated and has no gastro-intestinal disorder.

DISCUSSION

DR. SIGMUND S. GREENBAUM: Over a great part of the body the patient presents sheets of urticarial-like eruption in addition to the bullae and hemorrhagic blebs. There are no individual wheals such as are common to urticaria, and there is no real herpetic arrangement. The last case of this disorder I saw was in Darier's clinic; it was presented as a form of painful polymorphous bullous dermatitis of Brocq, which condition, of course, is now grouped entirely under the heading of dermatitis herpetiformis.

DR. FRANK C. KNOWLES: My co-workers and I have followed this patient for about five years. He has taken arsenic, but he seemed to have a certain idiosyncrasy for the drug and had to stop taking it. Some improvement from intravenous administration of calcium gluconate is becoming manifest.

DR. MARION B. SULZBERGER, New York: In my opinion this is undoubtedly a case of Duhring's disease with, as Dr. Greenbaum has said, polymorphous lesions. I think the large circinate, sharply circumscribed lesions are interesting on account of the possible connection between Duhring's disease and erythema annulare centrifugum of Darier. Recently several articles have been published which tend to prove that in cases of typical forms of Darier's erythema bullae sometimes develop and that there is probably a connection between Duhring's disease and Darier's annular erythema.

DR. JOHN H. STOKES: I feel as the other members do, that there is an intermediate picture of erythema multiforme, dermatitis herpetiformis and pemphigus, and I should like to point out one or two differential considerations which, I think, need to be gone into rather fully. In the first place, eruptions like the one exhibited by this patient may be produced by barbiturates. The eruption has been present for five years, during which time the patient has probably taken nearly every drug available. I think one should not forget the possibility of bullous lichen planus and bullous lupus erythematosus in disorders of this sort. If the eruption involved the extremities a little more I should give the latter diagnosis serious thought. The fact that this condition has been present for five years puts it in a group in which I have always been rather interested. I heard after I had seen the first case of this disorder that it had subsequently cleared up as a result of treatment with thyroid, and I suggest that this patient be given as much thyroid as he tolerates. Why thyroid caused the condition to clear up in my patient, I do not know, but on reliable authority I know that she has been nearly free from the disorder for five years, and she told me herself that she had been vastly improved as a result of the treatment.

DR. FRED D. WEIDMAN: Dr. Sulzberger anticipated my remarks. I wish to call attention also to the overlapping of the manifestations with those of erythema multiforme, to the remarkable symmetry of this eruption. It is true, Duhring's disease is roughly symmetrical, but I think it is not quite so strikingly symmetrical as this. A similar problem arose in the case of a patient who had made the rounds of the dermatologists in Philadelphia for many years and whose disorder had been diagnosed as Duhring's disease. He died in the Philadelphia General Hos-

pital. The terminal stage of his eruption was of the order of that exhibited by Dr. Ludy's patient, i. e., of the character of erythema perstans. The bullae presented by this patient were lacking; there were only vesicles. At necropsy bronchiectasis was demonstrated in both lungs. I think that the possibility of a focal infection should be considered in this case.

PATCHY ALOPECIA OF THE SCALP DUE TO LICHEN PLANUS. Presented by DR. REUBEN FRIEDMAN.

S. R., a woman aged 30, presents on the scalp, particularly over the anterior half, a number of pinkish, slightly scaly patches of alopecia of irregular size and shape. The hair all over the scalp can be easily extracted. On the trunk and upper extremities there is a generalized eruption of lichen planus, the follicular variety predominating. The lower extremities are involved to a less degree. The patient reports that a sudden eruption of reddish papules resembling goose flesh was first noticed on the abdomen on Jan. 11, 1936. This rapidly spread to the rest of the trunk and to the extremities. Two weeks later the patient noticed that she was losing much of her hair. Small bald spots were observed early in February. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I think Dr. Stokes was the first to present a case of this disorder—lichen planopilaris with cicatricial alopecia—before the society. I presented a case of a similar disorder some time ago as one of tuberculid with cicatricial alopecia. The patient's cutaneous condition cleared up as a result of treatment with gold sodium chloride, but the alopecia was, of course, permanent. Could the condition of the scalp be an acute form of sclero-atrophic lichen planus?

DR. JOHN H. STOKES: I think that this disorder falls within the group which Graham Little illustrated by three cases. I should like to see somewhat more typical lesions of lichen planus, but I did see some lesions resembling those of that disease on the abdomen. If, as in the case that I showed, one could see typical lesions and Wickham's striae about the wrists, I should feel more at ease about the diagnosis, but I have seen lichen planus so extensively follicular and yet so definitely lichen planus that I do not see why this patient's eruption is not within the range of variation of lichen planus.

DR. MARION B. SULZBERGER, New York: I agree with Dr. Stokes. I have seen a few cases of the disorder which Graham Little called lichen spinulosus with folliculitis decalvans and which is now termed lichen planus et acuminatus atrophicans. I have seen cases in which it was interesting to note that one could see at first spinous lesions on the scalp resembling those on the body and that these follicular lesions preceded the diffuse and scarlike alopecia. Probably the same follicular process seen on the glabrous skin without alopecia leads to the alopecia on the scalp. I do not know what the prognosis is for these lesions on the scalp; they certainly do not look as if hair would grow on the involved areas.

DR. JOHN H. STOKES: In a patient whom I have seen for five years the alopecia has been permanent.

DR. REUBEN FRIEDMAN: I think that some of the lesions, particularly those on the flanks, are definitely lichen planus. The entire eruption began in the manner of an acute goose flesh-like eruption, to use the patient's expression. I think that it was a lichen planus of a follicular type and that some of these follicular lesions eventually developed into the typical flat lichen planus. The patient has also lesions slightly suggestive of lichen planus on the buccal mucosa.

Book Reviews

Deliberationes Congressus Dermatologorum Internationalis IX-i. Budapest, 13-21 Septembris, 1935. Pp. 1005.

This book is an exceedingly interesting report of the proceedings of the congress. It gives the papers and discussions classified under the nine themes of the congress, as follows: (1) new investigations of the functions of the skin; (2) reciprocal relations and antagonisms between the skin and the internal organs; (3) allergy in dermatology and syphilology; (4) metabolic disturbances in cutaneous diseases; (5) effect of external causes on the frequency and form of cutaneous diseases; (6) the filtrable viruses in cutaneous diseases; (7) new results of the investigations of the pathology of tuberculosis; (8) therapy of syphilis; (9) criteria of the sanitation of syphilis.

The various titles indicate the comprehensiveness and fulness of the discussions of these formal themes. Over 400 pages are devoted to this section of the book, and the reports and discussions come from outstanding workers.

The second section is devoted to special papers given in conference and in meetings devoted to particular subjects, namely, conference on comparative dermatology, individual dissertations which are grouped under physiology, general pathology, general therapy, physical therapy, lymphogranuloma venereum (lymphogranulomatosis inguinalis), leprosy, tropical diseases, bacteriology and mycology, psoriasis and parapsoriasis, pathologic conditions of the hairs and nails, tumors, syphilis, gonorrhea and various unclassified papers.

The whole book comprises 1,005 pages. It is a magnificent exposition of the present state of knowledge in the field of dermatology.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H. W. Barber, President, 7, Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7, Devonshire Pl., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Paul A. O'Leary, Chairman, 102 Second Ave., S.W., Rochester, Minn.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.

AMERICAN DERMATOLOGICAL ASSOCIATION

John H. Stokes, President, 3800 Chestnut St., Philadelphia.
F. D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cleveland. Time: Dec. 5, 1936.

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

A, H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J. F. Wallhauser, President, Medical Tower, Newark.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of January, March, May, September and November.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Jack W. Jones, Chairman, 384 Peachtree St., Atlanta, Ga.
Winston U. Rutledge, Secretary, 332 W. Broadway, Louisville, Ky.
Place: Baltimore. Time: Nov. 17-20, 1936.

STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

Thomas J. Clark, Chairman, 400, 29th St., Oakland.
George V. Kulchar, Secretary, 450 Sutter St., San Francisco.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Maurice J. Strauss, Chairman, 41 Trumbull St., New Haven, Conn.
Edward A. Abbey, Secretary, 442 Temple St., New York.

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

LOUISIANA DERMATOLOGICAL SOCIETY

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P. Towle, President, 453 Marlborough St., Boston.
Rudolf Jacoby, Secretary, 270 Commonwealth Ave., Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Louis Tullipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg., Philadelphia.
L. G. Bembauer, Secretary, 5026 Jenkins Arcade Bldg., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

G. Warren Hyde, Chairman, 2501 W. Grand Blvd., Detroit.
Ruth Herrick, Secretary, 26 Sheldon Ave., Grand Rapids.

MINNESOTA DERMATOLOGICAL SOCIETY

L. H. Winer, President, 78 S. Ninth St., Minneapolis.
F. W. Lynch, Secretary, Lowry Medical Arts Bldg., St. Paul.
Time: First Wednesday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Charles P. Bondurant, President, 412 Medical Arts Bldg., Oklahoma City.
Darrell G. Duncan, Secretary, 914 Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

C. M. Griswold, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Galveston. Time: October.

LOCAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Leon Ginsburg, President, The Walbert, Baltimore.
Francis A. Ellis, Secretary, 104 W. Madison St., Baltimore.

Bronx Dermatological Society

Paul Gross, Chairman, 35 E. 84th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

George F. Price, President, 884 Lincoln Pl., Brooklyn.
Mortimer J. Cantor, Secretary, 907 St. Marks Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl L. Eaton, President, 40 North St., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Central New York Dermatological Society

George M. Fisher, President, 264 Genesee St., Utica.
Rudolph Ruedemann Jr., Secretary-Treasurer, 214 State St., Albany.

Chicago Dermatological Society

Max S. Wien, President, 104 S. Michigan Ave., Chicago.
Reuben Nomland, Secretary, 25 E. Washington St., Chicago.

Cincinnati Dermatological Society

Raymond G. Senour, President, Carew Tower, Cincinnati.
Leon Goldman, Secretary-Treasurer, Doctors Bldg., Cincinnati.

Cleveland Dermatological Society

John E. Rauschkolb, President, 1705 Medical Arts Bldg., Cleveland.
C. L. Cummer, Secretary, 1010 Hanna Bldg., Cleveland.

Detroit Dermatological Society

W. G. Wander, President, 509 Kresge Bldg., Detroit.
G. Warren Hyde, Secretary-Treasurer, 2501 W. Grand Blvd., Detroit.

Los Angeles Dermatological Society

Harry P. Jacobson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas W. Nisbet, Secretary, 65 N. Madison Ave., Pasadena, Calif.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Isidore Rosen, Chairman, 106 E. 54th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrook St., E., Montreal, Canada.

New England Dermatological Society

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

New York Academy of Medicine, Section of Dermatology and Syphilis

J. Gardner Hopkins, Chairman, 102 E. 78th St., New York.
David Bloom, Secretary, 135 E. 50th St., New York.

New York Dermatological Society

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

Omaha Dermatological Society

J. A. Borghoff, Chairman, 1319 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1113 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Vaughn C. Garner, Chairman, Germantown Professional Bldg., Philadelphia.
Thomas Butterworth, Secretary, 238 N. 5th St., Reading, Pa.

Pittsburgh Dermatological Society

Joseph J. Hecht, President, 506 Medical Arts Bldg., Pittsburgh.
Abraham Fisher, Secretary, 530½ Fifth Ave., McKeesport, Pa.

St. Louis Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: Second Wednesday of each month.

San Francisco Dermatological Society

L. R. Taussig, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.